

Behavioral Symptom Confusion: Distinguishing Rejection of Care,
Aggression, and Agitation in Persons with Dementia Living in the
Community

by

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ABSTRACT

Purpose

The purpose of this dissertation is fourfold: 1) to investigate the extent to which three common behavioral symptoms co-occur and whether the frequency of their co-occurrence can be replicated in another caregiver sample; 2) to examine the predictors of co-occurring behaviors; 3) to investigate the impact of these co-occurring behaviors on caregiver depressive symptomatology; and 4) to examine whether social support and caregiving mastery moderate the impact of behavioral symptoms on caregiver depression within each behavioral cluster.

Methods

This study involved a secondary analysis of the baseline data gathered in two completed community-based trials. Participants were recruited in Philadelphia region between December 2003 and March 2007 (Advancing Caregiver Training; ACT, N=272), and between March 2006 and June 2008 (Care of Persons with Dementia in their Environments; COPE, N=256), from media announcements and mailings by social agencies. Descriptive statistics, omnibus test, and logistic regression analyses were used.

Results

Of 272 dyads (ACT), the following combination of behaviors were identified based on the frequency of their occurrence: all three behaviors occurring together (N=106, 39%), agitation + aggression (N=65, 24%), agitation alone (N=41, 15%), agitation + rejection of care (N=35, 13%), rejection of care alone (N=5, 2%), aggression alone (N=3, 1%), rejection of care + aggression alone (N=1, 0%). This combination of behaviors was replicated in another sample (COPE). Using ACT, greater cognitive impairment was associated with ‘agitation + rejection of care’ and ‘all three behaviors’ while greater caregiver frustration was associated with ‘agitation + aggression’ and ‘all three behaviors.’ In a

combined data set of ACT and COPE (N=509), ‘all three behaviors’, ‘agitation + rejection’, and ‘agitation + aggression’ each had a positive association with caregiver depression whereas ‘agitation alone’ had no such association. Neither social support nor mastery significantly moderated the relationship between these combinations of behaviors and caregiver depression.

Conclusion

This study provides evidence that community-dwelling persons with dementia exhibit different combinations of behaviors that have distinct impacts on family caregivers. Findings suggest a continued need to obtain conceptual clarity that distinguishes among these three common behaviors to develop targeted treatments to alleviate the burdens associated with dementia-related behaviors.

Advisor: Laura N. Gitlin, PhD

Dedication

I dedicate this thesis to my mother Kim Sun Hwa, my father Choi Jong Soo, my wife An Ji Young, and my dear daughter Claire Dain Choi. I could not have accomplished this without their support and sacrifices.

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CHAPTER 1: INTRODUCTION

BACKGROUND

What is dementia?

Dementia is an umbrella term describing diseases and conditions characterized by a decline in memory and other cognitive skills that affect an individual's ability to perform everyday activities.¹

Dementia is classified as a major neurocognitive disorder in the latest *Diagnostic and Statistical Manual of Mental Disorders (DSM)* – 5.² As many as 5.2 million Americans suffer from dementia.³

Dementia, which is caused by damage to nerve cells in the brain, progresses slowly and irreversibly, leading to cognitive decline (e.g., memory loss, language difficulty, learning difficulty), behavioral and psychiatric disorders (e.g., agitation, delusions, depression), and declines in functional status (e.g., paying bills, managing medications, engaging in activities of daily living).¹

Types of dementia include Alzheimer's disease (AD), vascular dementia, dementia with Lewy bodies (DLB), frontotemporal lobar degeneration (FTLD), Parkinson's disease (PD) dementia, Creutzfeldt-Jakob disease, with AD accounting for the majority (60-80%) of the cases.¹ Some of the different types of dementia have unique behavioral symptom patterns.

The symptoms of dementia generally start with memory loss or other cognitive problems, and then lead to progressive difficulties effecting language, personality and behavior changes, visual disturbances, and sleep problems. As the disease progresses further, people with dementia may not recognize their family and friends, and in the final stages, may be completely dependent on others for ADL assistance such as eating, bathing, and dressing.

Dementia care in the community

Most persons with dementia live in the community and receive hands-on care provided by family caregivers.⁴ The costs related to this informal caregiving are enormous. In 2015, more than 15 million Americans provided an estimated 18.1 billion hours of unpaid care to their family members or relatives

with dementia.¹ This figure represents an average of 21.9 hours of care per caregiver per week or 1,139 hours of care per caregiver per year, which was economically valued at \$221.3 billion in 2015.¹

Caregivers of persons with dementia, on average, provide more extensive care for a longer time than do caregivers of older adults with other conditions.¹ 38 percent of all family caregivers of community-dwelling older adults with dementia provide ADL (e.g., bathing, dressing) and/or IADL (e.g., household chores, shopping, managing finances) care for 6 or more years.⁵ These costs are estimated to increase significantly as the numbers of older adults in the U.S. continue to grow.

Behavioral symptoms in dementia

Behavioral symptoms, sometimes referred to as neuropsychiatric symptoms (NPS) or behavioral and psychological symptoms of dementia (BPSD), affect persons with dementia nearly universally across dementia stages.⁶ Individual behavioral symptoms often occur in clusters or syndromes. This dissertation focuses on the three behaviors that are known to have fairly consistently appeared in the ‘hyperactivity/agitation’ syndrome.⁷

Rejection of care

Rejection of care has been referred to as “*the repertoire of behaviors with which persons with dementia withstand or oppose the efforts of a caregiver.*”⁸ This behavior has also been referred to as noncompliance, uncooperative behavior, or resistiveness to care.⁹ Evidence suggests that rejection of care typically occurs when persons with dementia misinterpret caregiver’s care attempts as a threat.^{10,11} Also, there is some research to suggest that rejection of care could lead to aggressive behaviors, particularly when caregivers persist in attempting to provide care despite the refusal of the person with dementia.^{8,12,13}

Rejection of care is among the behavioral symptoms that are most prevalent and troublesome to caregivers. In a randomized controlled trial targeting 272 community-dwelling caregivers and people with dementia, ‘refusing help’ was identified by family caregivers as the most distressful symptom among a wide range of problem behaviors.¹⁴ Brodaty et al.¹⁵ reported that nursing home staff members cited patient’s being ‘stubborn or resistive’ as one of the five attributes most difficult to cope with. Also, a

survey of 110 nursing home physicians reported that ‘resisting care’ was the most frequently observed symptom (71%).¹⁶ Factors found in a previous study to be associated with rejection of care are dementia severity, medical conditions, and psychological symptoms such as delusion, hallucination, or depression.¹⁷

Aggression

Aggression has been referred to as “*an overt act, involving the delivery of noxious stimuli to (but not necessarily aimed at) another object, organism or self, which is clearly not accidental.*”¹⁸ Unlike rejection of care, aggression presupposes an intent to harm others (or self),^{17,19} and may include verbal or physical actions directed at a person or object.

Aggression occurs more frequently among older adults with cognitive impairment than those with no cognitive impairment.²⁰ Aggression is associated with severe caregiver stress, aggressive caregiver reaction, psychotropic drug use, and a risk for institutionalization.¹⁰ Estimated prevalence of aggression varies greatly depending on definition, sample, and setting, but for nursing home population, physical aggression varied from 17%²¹ to 46%,²² and to 57%,²³ and verbal aggression varied from 50%²² to 69%.²⁴ A community-based longitudinal study has determined the prevalence rate of aggression to be 41% (physical aggression 19%; verbal aggression 33%) over 24 months.¹⁹

As with other behavioral symptoms, aggression can be triggered by an interaction of multiple factors. Possible causes include caregiver burden, care receiver pain, and low quality of caregiver-person with dementia relationship.¹⁹

Agitation

Agitation is also variably defined in the literature and on measurement tools but typically refers to “*inappropriate verbal, vocal, or motor activity that is not explained by needs or confusion per se.*”²⁵

Agitation impairs the quality of lives for persons with dementia and their family, increases the likelihood of institutionalization of persons with dementia, and often leads to physical/chemical restraints.^{25–29} The prevalence of agitation varies widely across studies. Chan et al.³⁰ reported that 45% of community-dwelling elderly people with dementia had at least one symptom of agitation over one month

period while almost all (90%) community residing elderly people attending senior day-care centers displayed at least one agitated behavior every week.³¹ Some of the associated factors include medical conditions, cognitive impairment, pain, and inability to communication.^{32,33}

Conceptual confusion concerning agitation-type behaviors

Despite the large number of studies on agitation in dementia, there is confusion regarding the definition and conceptual boundaries of agitation. In a pioneering work to map out an instrument to operationalize agitated behaviors in persons with dementia, Cohen-Mansfield³⁴ categorized aggressive behaviors such as hitting, kicking, scratching, or cursing as one of the three types of agitated behaviors (i.e., aggressive behaviors, physically nonaggressive behaviors, verbal behaviors).

In addition to the problem of including aggressive behaviors under the overarching category of agitation, the definition of agitation also overlaps with the concept of rejection of care. Rosen et al.³⁵ in their proposal of the guideline to assess agitation defined agitation as *‘vocal or motor behavior that is either disruptive, unsafe, or interferes with the delivery of care in a particular environment’*, which is clearly a description of rejecting behaviors of a person with dementia.

The Neuropsychiatric Inventory (NPI),³⁶ the most widely adopted and recommended clinical instrument for assessing behavioral symptoms in dementia,³⁷ does not distinguish agitation from aggression but instead has a domain named ‘agitation/aggression’ which evaluates aggressive behaviors as well as agitated behaviors. What makes this more complicated is that some of the items of ‘agitation/aggression’ domain including the screening questions describe rejection of care behaviors (e.g., “Is the patient uncooperative?”, “Is the patient hard to handle?”, “Does the patient resist activities such as bathing or changing clothes?”).

Why is differentiation of behaviors important?

The distinction among rejection of care, aggression, and agitation is important because they may each have different underlying etiologies, thus requiring different nonpharmacologic treatments. For example, agitated behaviors (e.g., pacing, picking at things, repetitious mannerism) in nursing home most

occur when the person with dementia is alone and not involved in any activity.³¹ This may be the manifestation of boredom, loneliness, or need of stimulation that persons with dementia experience in nursing home and can be treated with provision of different types of stimuli (e.g., music, social stimuli, simulated social stimuli, and structured activities). However, agitated behaviors (i.e., rejection of care) during interactions with a caregiver, especially in the context of ADL care, should be managed by enhancing communication techniques or modifying care approaches because they often result from communication deficits or inability to understand others by the person with dementia.^{13,38–40}

Similarly, aggressive behaviors, which usually follow rejecting behaviors of a person with dementia during care activities initiated by a caregiver, may be managed by preventing rejection of care from escalating into combative or abusive behaviors.^{10,41,42} Some of the preventive techniques include watching for warning signs of escalation, delaying the care, distracting the person with dementia, and explaining every process of care in a reassuring and gentle voice.⁴³

Distinguishing among related but possibly distinct behavioral symptoms

Recent research has suggested that behaviors typically subsumed under agitation such as rejection of care, aggression, or agitation,^{44–46} may be conceptually distinct and should be examined separately.

The Agitation Definition Work Group (ADWG) consisting of the International Psychogeriatric Association (IPA) members and its affiliates discussed the relationship between agitation and aggression, and concluded that these are overlapping but not identical concepts.⁴⁷ In a survey to develop a consensus definition of agitation, 66% of 557 IPA members and its affiliates who responded to the survey considered agitation and aggression as overlapping concepts, 32% as distinct concepts.⁴⁷ Since agitation (e.g., excessive motor activity) may occur in the absence of aggression, it would be important to compare agitation with and without aggression to further elucidate their relationship.

Furthermore, based on the evidence that agitation and aggression may be prevalent even when measured separately,^{48,49} the agitation/aggression domain of the most common measure of behavioral symptoms, the NPI, was in its most recent iteration, considered as two distinct domains.⁵⁰

Some researchers have also suggested that rejection of care may also be distinguished from agitation and aggression. Volicer et al.¹³ identified four distinct groups of persons with dementia using data from the Veterans Administration's long-term care facilities: those rejecting care, those with agitation, those manifesting both rejecting and agitated type behaviors, and those with neither type of behaviors. The authors concluded that agitation and rejection of care, although co-occurring, had a different relationship to severity of dementia.

In a randomized controlled trial of a nonpharmacological intervention, Gitlin et al.¹⁴ found that rejection of care was the most common behavioral symptom (15.4%) that was targeted by caregivers as distressful and for which they would want help managing. In this study, caregivers were asked to identify a target problem behavior which they found most troublesome. The prevalence of caregivers who reported verbally aggressive behavior, agitated behavior, and physically aggressive behavior as most upsetting were 7.9%, 5.0%, and 2.9% respectively. This indicates that caregivers considered these behaviors as distinct and their reactions to their occurrences varied.

The distinction between rejection of care and aggression type of behaviors is not clear-cut and has been rarely made in the literature. Some investigators suggest that the underlying intent of a person with dementia should be considered when labeling either type of behavior.^{9,41} For example, if a person with dementia exhibited aggressive behaviors (i.e., verbally and/or physically abusive behavior toward a caregiver) during personal care because he or she misperceived the caregiver's care attempt as threat, the behavior should be rejection of care and not aggression.

Yet, in an observational study of physically aggressive behaviors, Bridges-Parlet et al.¹² suggested that behaviors may occur on a continuum such that agitated behaviors occurred first, and, if not recognized by caregivers, and attempts at caregiving persist then behaviors could progress to verbally aggressive, and then physically aggressive behaviors.

Further support for the distinction between rejection of care and aggression comes from a factor analysis of a Rating Scale for Aggressive Behavior in the Elderly (RAGE).¹⁸ Factor analysis of 19 items revealed three factors: verbal aggression, physical aggression, and antisocial behaviors, and the rejection

of care item ('uncooperative/resisted help') did not load strongly with any of those factors, suggesting that rejection of care may be a distinct behavior.

Dementia caregiving and caregiver's well-being

Caring for people with dementia places enormous emotional, physical, and financial stress on family members who provide care. As the disease progresses the level of supervision and personal care needed for a person with dementia increases to the point that assistance is required for even the most basic ADLs (e.g., getting in and out of bed, getting to and from the toilet, managing incontinence and feeding). The chronic stress of caregiving has been associated with negative impact on several dimensions of caregiver health including self-reported health,⁵¹ health symptoms,⁵² days of illness,⁵³ and mortality.⁵⁴ Particularly dementia caregiving is associated with negative caregiver mental health compared to caregiving for persons with other physical impairments.⁵⁵ Rabins, Mace and Lucas⁵⁶ reported that a majority of caregivers of persons with dementia develop significant psychological distress including chronic fatigue, frustration, and depression.

Behavioral symptoms and caregiver's psychological well-being

In addition to the intensive support required for a person with dementia, personality and behavior changes of persons with dementia (e.g., agitation, wandering, repetitive activity), which often occur as the disease progresses, can result in increased emotional stress and depression in family caregivers.¹

Behavioral symptoms of dementia are often cited as predictors of caregiver burden and depression.⁵⁷ Evidence suggests that the mental health of caregivers is more affected by behavioral symptoms than cognitive impairments.⁵⁴ In a study that examined the longitudinal impact of behavioral symptoms on caregiver burden and stress, Gaugler et al.⁵⁸ reported that increase in behavioral symptoms predicted, even more so than cognitive impairments and ADL dependencies, increase in caregivers' subjective stressors (i.g., role overload) and depression. Similarly, caregivers who report greater emotional stress related to behavioral symptoms are more likely to place persons with dementia to nursing homes.⁵⁹

While many researchers have consistently demonstrated the links between behavioral symptoms of dementia and negative caregiver's mental health (e.g., depression, burden),^{57,60} these studies have several limitations. First, most studies have conceptualized and operationalized behavioral symptoms as a single construct and have not examined specific symptoms or symptom groups. Second, with few exceptions,⁶¹ studies have not examined the unique contributions of each behavioral symptom to caregiver distress.

When examining associations of behavioral symptoms and caregiver outcomes, it is important that a syndromic approach be taken since different symptom groupings or syndromes may have differential impacts on caregiver outcomes. By differentiating symptom groupings, it may be possible to determine whether there are individual symptom clusters that are most stressful for caregivers, an opportunity to target interventions. However, how behavioral symptoms are classified or grouped has been a contentious issue and there is little consensus. Investigators have taken various approaches (e.g., observation, latent class analysis) in classifying behavioral symptoms using various measures (e.g., NPI, BEHAVE-AD), which has resulted in considerable heterogeneity in classifying these symptoms.^{37,62–65}

Missing from previous work has been the understanding of behavioral symptoms as occurring in a particular context that triggers or contributes to their occurrences. One such context is care provision and whether behaviors occur when certain care routines are performed. In a systematic review of the literature that examined the association between behavioral symptom clusters and caregiver burden or depression,⁵⁷ of 35 research articles, no study differentiated behaviors that occurred during caregiving from behaviors that occurred when persons with dementia were alone.

Failure to consider contextual factors in measuring behavioral symptoms such as information as to whether behaviors occur during caregiving activity or not may be limiting our understanding of how and when behaviors occur and their differential impact on caregiver's burden and depression. For example, a caregiver may feel frustrated when his or her efforts to help their relative with the basic needs of daily living are rejected (e.g., walking out of the room, pushing person away). The emotional toll of the family member's rejecting behavior on the caregiver could be much more profound when the family

member with dementia is the caregiver's spouse that the caregiver spent a lifetime with and feels emotionally invested in. On the other hand, behavior like wandering, or restlessness, which do not necessarily involve an interaction with a caregiver, may not be as emotionally disturbing to caregivers, particularly if there is not a safety concern. As such, the context in which behaviors occur may be differentially troublesome or upsetting to caregivers.

CONCEPTUAL MODEL

The dissertation draws upon the conceptual model that links the interaction between factors related to person with dementia, caregiver, and environment with behavioral symptoms,⁶⁶ and the stress process model.⁶⁷ The first conceptual framework⁶⁶ maps the relationship of neurodegenerative processes and behavioral outcomes. According to this model, behavioral symptoms are likely to result from several contributory factors and their interaction (Figure 1). Central to the emergence of behaviors is the neurodegeneration process which disrupts brain circuitry involved in affect and behavior. Additionally, 3 other factors (person with dementia, caregiver, and environmental factors) and their interactions with each other contribute to behavioral symptoms by increasing vulnerabilities of the person with dementia to stressors. These factors may contribute to behavioral symptoms independently or in conjunction with each other.

Neurodegeneration associated with dementia

The disruption in neurocircuitry involved in executive function, motivated behavior, and inhibitory control could result in behaviors of dementia such as agitation and aggression.⁶⁸ Stewart et al.⁶⁹ systematically studied the role of executive dysfunction in the manifestation of rejection of care in dementia and found that executive impairment is an independent predictor of rejection of care among persons with dementia living in a nursing home setting. Impaired ability to understand caregiver's intent and goals is thought to contribute to rejecting behavior in persons with dementia.¹³

Person with dementia factors

Acute medical conditions (e.g., pain, undiagnosed illnesses),⁷⁰ unmet needs (sleep problems, loss of control, or lack of social activities), pre-existing personalities and psychiatric illnesses⁷¹ may affect the

development of behavioral symptoms. For example, pain resulting from conditions such as constipation, unrecognized fracture, or arthritis may all cause rejection of care,⁷⁰ aggression,⁷² or agitation³⁴ in persons with dementia.

Caregiver factors

Factors such as negative caregiver communication style (e.g., screaming, impatience, or ignorance), coping strategies, stress or depression may trigger or exacerbate behavioral symptoms of persons with dementia.⁴⁵ For example, Williams et al.⁷³ videotaped interactions between nursing staff and residents with dementia during ADL care and found that elderspeak (infantilizing communication used by caregiver) the occurrence of rejection of care (or agitated/aggressive behaviors during ADL care) significantly increased when staff used elderspeak in comparison to normal talk or silence.⁷³

Environmental factors

Internal and/or external stimuli may cause anxiety or rejection of care in persons with dementia as their abilities to process and respond to environmental stimuli decrease progressively.⁷⁴ Potential stressors include changes in daily routine, too many competing stimuli, lack of stimuli, and tasks or activities that do not match the capabilities of the person with dementia.^{66,75} For example, the presence of loud volume radio or television may make persons with dementia anxious first, and if the stress is unrelieved and exceeds the person with dementia's capacity to cope and adapt, behaviors such as agitation, rejection, or aggression may emerge.⁷⁴ For this dissertation, environmental factors were not considered due to data limitation.

This conceptual framework was used in this study to guide the selection of predictors of behavioral symptoms, which in turn can lead to an understanding of the meanings of behaviors, from which to develop management strategies for behaviors.

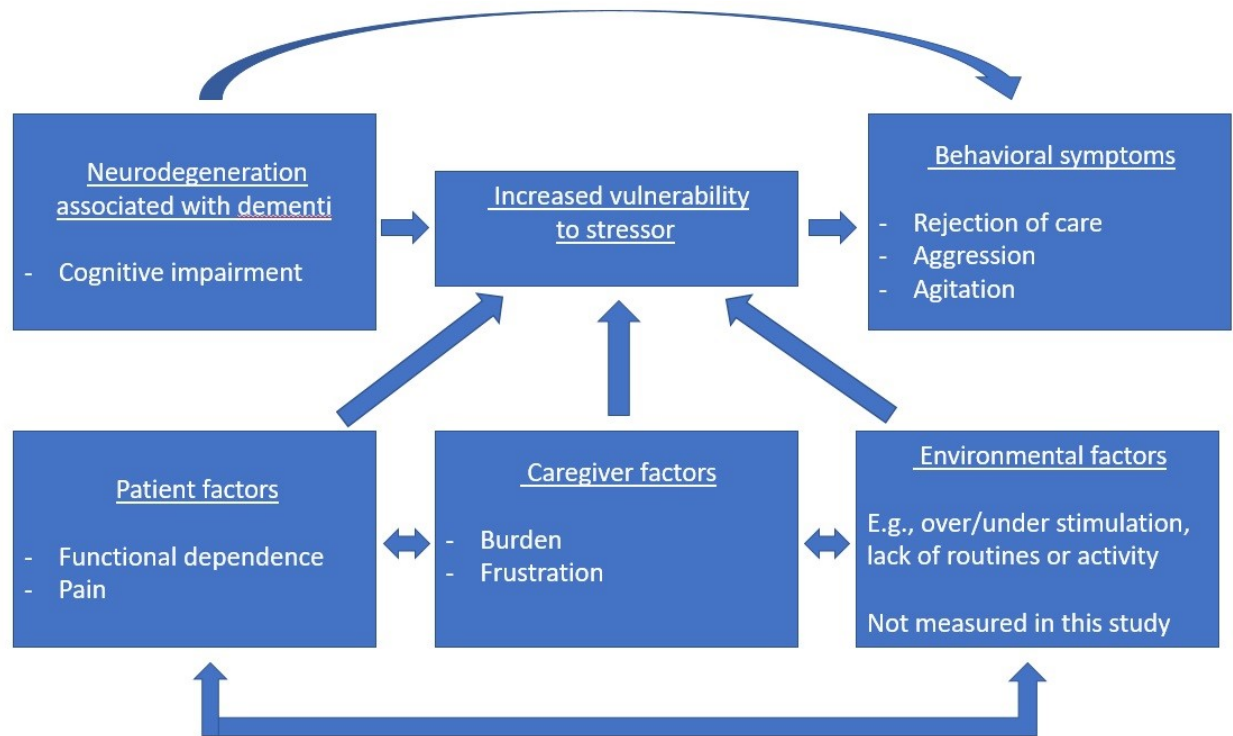


Figure 1. Conceptual model linking the interaction between neurodegeneration, person with dementia, caregiver, and environmental factors to the emergence of behavioral symptoms.⁶⁶ Figure displays variables in ACT.

Stress process model

This dissertation is also guided by the use of the stress process model (Figure 2).^{67,76} According to this model, the stress process has three components. *Stressors* are the challenging conditions experienced by caregivers (e.g., behavioral symptoms in persons with dementia). *Outcomes* refer to the consequences of stressors such as the effects of behavioral symptoms on caregivers' well-being (e.g., depression). For example, a caregiver who cares for his/her relative with dementia who exhibits wandering behavior may feel burdened due to high level of vigilance or surveillance the behavior may require on the caregiver's part. *Moderators* are the third component which may serve as buffers of stress.^{67,77–79} The model suggests that social support and mastery are the resources that may regulate the impact of stressors on emotional well-being. That is, caregivers who lack social support and/or caregiving mastery (perceived competence within the caregiving role) will experience poor health outcomes such as depression.

The study examines the relationship of the four behavioral clusters (i.e., objective stressors) to caregivers' self-reported depressive symptoms (i.e., health outcome) while controlling for other important factors (e.g., background characteristics of dyads, cognitive status, ADL function, and relationship quality of dyads). Also examined is whether the relationship between a behavioral cluster and caregiver's clinical depression is moderated by levels of social support and caregiving mastery (Figure 2).

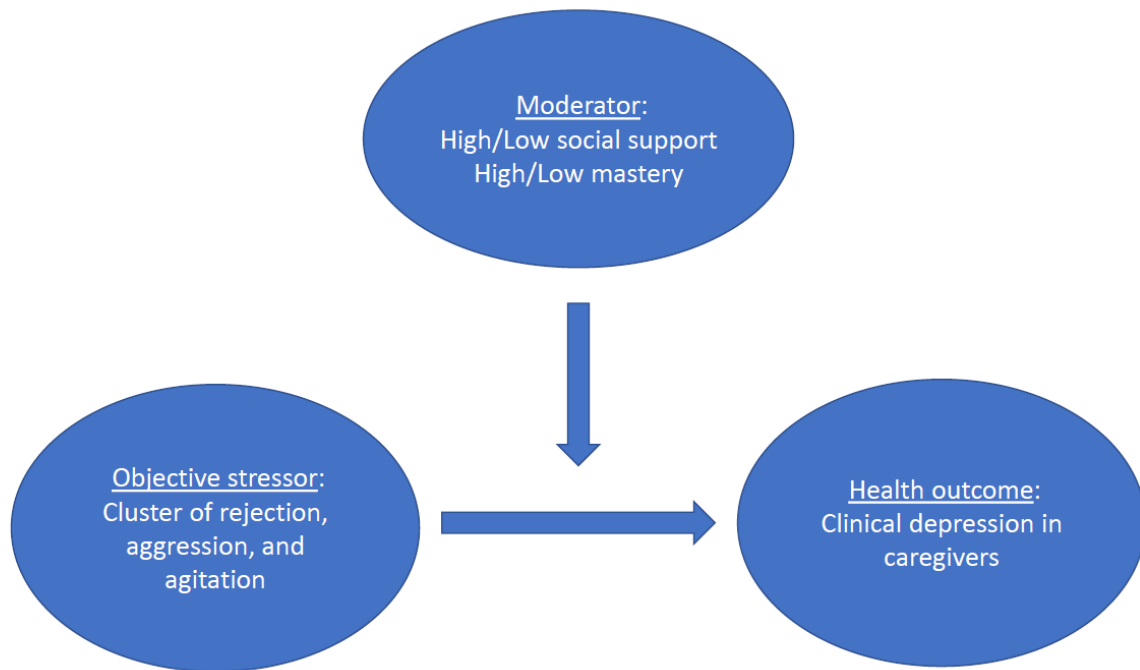


Figure 2. The relation of stressors to health outcome. Figure displays variables in the combined data sets of ACT and COPE.

Information that can clarify relationships between behavioral clusters of rejection, aggression, and agitation and caregivers' depressive symptoms could lead to development of interventions that can be tailored and delivered to the vulnerable caregivers of the persons with dementia exhibiting certain combinations of co-occurring behaviors.

SUMMARY

Dementia is a growing public health problem. As the segment of the U.S. population age 65 and older increases rapidly, so too will the numbers of people with dementia. The number of older adults with dementia in the U.S. is projected to nearly triple from 5.1 million in 2015 to 13.8 million in 2050.⁴

Although a recent prospective cohort study of U.S. adults reports a decline in the age-specific incidence of dementia in the U.S. between 2000 and 2012,⁸⁰ the dramatic aging of the population signals that prevalence rates will remain high. As most persons with dementia receive care at home from family or friends, the impact of the disease on these individuals is profound and includes economic, emotional and physical consequences.^{4,81} As to the financial burden, in 2015, Americans provided 18.1 billion hours of unpaid care to people with Alzheimer's and other dementias. The total costs of health care, long-term care and hospice for all individuals with dementia are estimated to be \$236 billion in 2016.

Along with cognitive and functional declines, behavioral symptoms (e.g., agitation, wandering) are the hallmark of dementia. Nearly all individuals with dementia will exhibit one or more behavioral symptoms over the course of the illness.⁸² These symptoms have been associated with significant distress for caregivers as well as for persons with dementia,^{83,84} early nursing home placement,³⁰ increase in health care costs,⁸⁵ faster disease progression,⁸⁶ and increased risks for morbidity and mortality.⁸⁷

Behavioral symptoms may have more negative impact on the caregiver's mental well-being than cognitive or functional impairments.^{88,89} For example, caregivers in a nursing home setting who experienced violent behaviors by residents directed toward them reported powerlessness, sadness, anger, and feelings of insufficiency as the most dominant reaction to the behaviors.⁹⁰ Depression is particularly common among dementia caregivers with the approximate prevalence rate of 40 percent in family caregivers of persons with dementia compared with 5 to 17 percent of non-caregivers of similar ages.⁹¹ Studies suggest that the intensive care required for behavioral symptoms of the person with dementia can adversely affect the caregiver's psychological well-being.^{88,92,93} This association between behavioral symptoms and depression in caregivers was reported to be mediated by the caregiver's subjective appraisal of the stress related to behavior management.^{78,79}

Various factors may contribute to or be a trigger of behavioral symptoms, including interactions between the factors related to persons with dementia, caregivers, and environmental conditions.⁶⁶ Understanding the modifiable factors that may lead to specific behavioral symptoms and differential

outcomes of certain behavioral symptoms on caregivers in order to improve treatment approaches in dementia care is paramount.

Behavioral symptoms often co-occur and tend to be lumped together and are not well delineated . One of the most frequently occurring and fairly consistently delineated behavioral types is agitation. Agitation-type behaviors may include a wide range of behaviors (e.g., restlessness, pacing, repetitive questioning) and including but not limited to the three that form the focus of this dissertation (rejection of care, aggression, and agitation). Agitation has been defined differently depending upon its measurement. The Cohen-Mansfield Agitation Inventory, one of the most widely used instruments to measure agitated-type behavioral symptoms in dementia, defines agitation as ‘inappropriate verbal, vocal, or motor activity that is not judged by an outside observer to result directly from the needs or confusion of the agitated individual.’³⁴ It is concerning, however, that in most measures, the definition of agitation is broad and appears to encompass distinct behavioral manifestations.

Two behaviors typically subsumed under agitation is rejection of care and aggression. Rejection of care has been defined as the ‘repertoire of behaviors with which persons with dementia withstand or oppose the efforts of a caregiver.’⁹⁴ Rejection of care behaviors may include screaming, hitting, and/or kicking that occur during the act of helping with self-care or activities of daily living (ADL). Rejection of care can manifest itself as well as an aggressive form of behavior occurring in the context of caregiving⁹⁴ and thus its distinction with aggression can be blurred. Aggression, on the other hand, has been defined as an ‘overt act, involving the delivery of noxious stimuli to (but not necessarily aimed at) another object, organism or self, which is clearly not accidental.’¹⁸ Aggression covers a range of different behaviors, some of which overlap with agitation or rejection of care. For example, Keene et al. included ‘resistance’, ‘refusing to speak’, and ‘general irritability’ as aggressive behaviors.¹⁰

The conceptual distinctions among these three behaviors has not been made and current measures either group behaviors under one rubric or do not fully explicate one from the other. Each behavior may pose a different level of risk to the person with dementia and caregiver and may contribute differentially to quality of life. It is unclear if these three behaviors co-occur, whether there is a temporal

order to their occurrence and the relationship of each to the other and other factors. Also the distinct contributions of each of these behaviors to other health-related outcomes and caregiver well-being are unclear. It may be, for example, that rejection of care impacts caregivers more negatively than other agitated-type behaviors whereas aggression may place the person with dementia and their caregivers in harm's way.

There have been only a few previous attempts to distinguish these behaviors or their possible differential effects on caregiver well-being. For example, Hurley et al.⁹⁵ argued that the term 'agitation' should be reserved for behaviors that occur when a person with dementia is alone and any inappropriate behaviors that occur within the context of caregiving should be named 'rejection of care'. Ishii et al.¹⁷ differentiated rejection of care and aggression based on the intent of the person with dementia. According to these authors only the behaviors with the underlying intent to harm others are aggression, and self-defensive behaviors should be rejection of care. Furthermore, the majority (98%) of 557 psychogeriatric clinicians who responded to a survey asking about the definition of agitation reported that agitation and aggression may be overlapping but not the same behavior.⁴⁷

It is also not clear whether these three behaviors are distinguishable by their different relationships with factors that may contribute to the emergence of behaviors. Previous studies have reported inconsistent results regarding the association of rejection of care, aggression, and agitation and contributory factors of behavioral symptoms,^{17,45} which makes it difficult to identify specific factors that are consistently associated with one behavior. These inconsistent or even conflicting findings may be related to failure to employ a system of behavior categorization that considers a context in which behaviors occur.

Distinguishing among rejection of care, aggression, and agitation is essential in formulating treatment strategies for persons with dementia because each of these three behaviors may have different contextual etiologies warranting different treatment approaches. For example, verbal agitation resulting from boredom can be alleviated by providing persons with dementia with social stimuli,⁹⁶ while rejection of care (e.g., verbal agitation during intimate care) may be managed by better caregiver communication

(e.g., explain every step of care to person with dementia slowly in simple sentences). Similarly, aggressive behaviors, which may follow a rejection of care episode or be encompassed in rejecting behavior,¹² may be prevented by recognizing rejection of care and keeping the behavior from escalating into combative behaviors.¹⁹

To date, no study has differentiated and examined the independent occurrences and co-occurrences of rejection of care, aggression, and agitation in persons with dementia living in the community and whether certain behaviors and/or their combination impact caregiver depression more than others. Thus, the purpose of this dissertation was fourfold: 1) to investigate the extent to which behaviors co-occur in one study and whether the combination and frequency by which they co-occur can be replicated in another caregiver sample; 2) to examine the predictors of individual behavioral symptoms and their combinations (e.g., agitation alone; agitation plus aggression; agitation plus rejection of care; all three behaviors); 3) to investigate whether individual behavioral symptoms and/or their combinations have a differential impact on caregiver depressive symptomatology; and 4) to examine whether social support and caregiving mastery moderate the impact of behavioral symptoms on caregiver depression within each behavioral cluster. For this study, data from two completed community-based trials that investigated behavioral symptoms and physical function of persons with dementia were used: (1) Project ACT,¹⁴ which tested the effectiveness of a multicomponent nonpharmacological home-based intervention to reduce behavioral and psychological symptoms of dementia and associated caregiver distress, and (2) Project COPE,⁹⁷ which tested the effectiveness of a nonpharmacological biobehavioral environmental intervention to address functional and behavioral challenges of persons with dementia.

SPECIFIC AIMS

Aim 1 - Determine whether rejection of care, aggression and agitation occur independently of the other and also the extent to which they co-occur in the past month before examination in persons with dementia living in the community (ACT trial data).

Prediction – Rejection of care, aggression, and agitation will co-occur in most persons with dementia (ACT trial data). Aggression will not occur independently of rejection of care or agitation. This aim will establish the prevalence of different combinations of behaviors (e.g., agitation plus aggression; agitation plus rejection of care; aggression plus rejection of care; and agitation, aggression and rejection of care).

Aim 2 - Evaluate whether the behavioral clusters differ with regard to factors associated with persons with dementia (cognitive impairment, ADL function, pain) and their caregivers (frustration and burden) (ACT trial data).

Prediction – Behavioral clusters will be associated with different factors, although given the lack of previous research in this area, it is not possible to hypothesize or predict with specificity.

Aim 3 - Determine if the prevalence of behavioral clusters in the past month identified in a sample from one trial (ACT) can be replicated in another sample of community-dwelling persons with dementia (COPE trial).

Aim 4 – Assess whether behavioral clusters in the past month have a differential impact on caregiver depression after controlling for potential confounders (e.g., background characteristics of dyads, cognitive status, functional status, etc.). Upon positive finding of Aim 3, ACT and COPE data sets will be combined for this analysis.

Prediction – Caregivers of persons with dementia who exhibit all three behaviors will be more likely to be clinically depressed than caregivers of persons with dementia who exhibit one or two co-occurring behaviors.

Aim 5 – Investigate whether the association between behavioral clusters and caregiver depression is moderated by psychosocial resources (social support and caregiving mastery).

Prediction – The relationship between behavioral clusters and caregiver depression will be moderated by social support and caregiving mastery such that those with low social support and mastery will be more likely to be depressed. For this analysis, The combined data set will be used.

SIGNIFICANCE

This study highlights the importance of three common and disturbing behavioral symptoms and the extent to which they occur independently or jointly. Although these behaviors have not been carefully delineated in the literature, recognizing these behaviors as potentially discrete clinical phenomenon and understanding if they co-occur is important in that each behavior may have a different set of contributory factors and hence require distinct clinical interventions. This study is also significant because the associations between these three behaviors and caregiver depressive symptoms and the mechanisms (i.e., moderating effects) by which they are associated have not previously examined.

This dissertation will contribute to the body of scientific knowledge on dementia, behavioral symptoms and caregiver distress by determining factors that may be uniquely related to each behavioral type and their possible co-occurrences as well as whether any behavior alone or in combination differentially impacts caregiver well-being. This knowledge is important in that it may shed light on the underlying causal mechanisms of different clusters of behaviors, which then could be used to develop etiologically-based therapeutic interventions.

Also, certain behavioral symptoms may result in more depression for the caregiver as they may cause more upset and frustration. This current study may inform efforts to target treatment for caregivers who are at risk for or who have depression by determining whether certain behavioral clusters of rejection, aggression, and agitation differentially impact well-being.

Finally, discerning co-occurring behavioral groups of rejection, aggression, and agitation may aid in the design of targeted interventions to assist caregivers in managing these behaviors, which may in turn enhance their mental well-being.

INNOVATION

The innovation in this study lies in its attempt to disentangle the pattern of occurrences of three common dementia-related behaviors (e.g., conceptualization of behaviors occurring within the context of caregiving vs. behaviors occurring when persons with dementia are alone) as well as their impact on the

caregiver. This study also considers how such behavioral clusters may have different relationships with contributory factors and differential impact on the caregiver outcome (i.e., depressive symptoms). To the best of my knowledge, this study is the first to examine co-occurrences of rejection of care, aggression, and agitation while applying clear distinctions among them. An understanding of the co-occurrences among these behaviors and their relationships with different clinical variables may help inform the design of targeted interventions for caregivers.

In addition, although there have been attempts to discern rejection of care from similar behaviors (i.e., agitation and/or aggression), those studies were exclusively conducted on persons with dementia in a nursing home setting and no such attempt has been made among persons with dementia living in the community.⁹⁸ This dissertation uses data from two randomized-controlled trials with a combined sample size of over 509 community-dwelling persons with dementia. Examination of the occurrences of these behaviors in the community, where most dementia care is provided, would help fill this gap in the literature.

Finally, this study is the first investigation of indirect paths that may link different combinations of occurrences of rejection, aggression, and agitation and clinically significant caregiver depressive symptoms. Findings may help target treatment efforts more effectively for person with dementia and caregiver dyads.

DISSERTATION ORGANIZATION

This dissertation consists of five chapters. Chapter one provides an overview of the study including a description of background, the purpose and specific aims, the conceptual frameworks, significance, and innovation. Chapter two is a systematic review of how rejection of care, aggression, and agitation are described and operationalized in existing measures of dementia-related behaviors, and provides recommendations for distinguishing these behaviors in measurement scales. Chapter three examines the relationships between behavioral different clusters of rejection of care, aggression, and

agitation and various contributory factors of behavioral symptoms. Chapter four explores the differential impact of behavioral clusters on caregiver depression, and a possible moderation effect of social support and caregiving mastery on these associations. Chapter five provides a summary of findings and discusses study strengths and limitations, and implications.

REFERENCES

1. 2016 Alzheimer's disease facts and figures. *Alzheimer's Dement.* 2016;12(4):459-509. doi:10.1016/j.jalz.2016.03.001.
2. Association AP, others. *Diagnostic and Statistical Manual of Mental Disorders (DSM-5®)*. American Psychiatric Pub; 2013.
3. Hebert LE, Weuve J, Scherr PA, Evans DA. Alzheimer disease in the United States (2010--2050) estimated using the 2010 census. *Neurology.* 2013;80(19):1778-1783.
4. Callahan CM, Arling G, Tu W, et al. Transitions in care for older adults with and without dementia. *J Am Geriatr Soc.* 2012;60(5):813-820. doi:10.1111/j.1532-5415.2012.03905.x.
5. Kasper JD, Freedman VA, Spillman BC, Wolff JL. The Disproportionate Impact Of Dementia On Family And Unpaid Caregiving To Older Adults. *Health Aff (Millwood).* 2015;34(10):1642-1649. doi:10.1377/hlthaff.2015.0536.
6. Lyketsos CG, Lopez O, Jones B, Fitzpatrick AL, Breitner J, Dekosky S. Prevalence of Neuropsychiatric Symptoms Results From the Cardiovascular Health Study. *Jama.* 2002;288(12):1475-1483. doi:10.1001/jama.288.12.1475.
7. Lyketsos CG, Carrillo MC, Ryan JM, et al. Neuropsychiatric symptoms in Alzheimer's disease. *Alzheimer's Dement.* 2011;7(5):532-539. doi:http://dx.doi.org/10.1016/j.jalz.2011.05.2410.
8. Mahoney EK, Hurley AC, Volicer L, et al. Development and testing of the Resistiveness to Care Scale. *Res Nurs Health.* 1999;22(1):27-38.
9. Ishii S, Streim JE, Saliba D. A conceptual framework for rejection of care behaviors: review of literature and analysis of role of dementia severity. *J Am Med Dir Assoc.* 2012;13(1):11-12. doi:10.1016/j.jamda.2010.11.004.
10. Keene J, Hope T, Fairburn CG, Jacoby R, Gedling K, Ware CJ. Natural history of aggressive behaviour in dementia. *Int J Geriatr Psychiatry.* 1999;14(7):541-548.
11. Potts HW, Richie MF, Kaas MJ. Resistance to care. *J Gerontol Nurs.* 1996;22(11):11-16. <http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id=8954387&retmode=ref&cmd=prlinks%5Cnpapers3://publication/uuid/4993A9BD-298D-4E5F-9F00-097BEC2C3A2F>.
12. Bridges-Parlet S, Knopman D, Thompson T. A descriptive study of physically aggressive behavior in dementia by direct observation. *J Am Geriatr Soc.* 1994;42(2):192-197.
13. Volicer L, Bass EA, Luther SL. Agitation and Resistiveness to Care Are Two Separate Behavioral Syndromes of Dementia. *J Am Med Dir Assoc.* 2007;8(8):527-532. doi:10.1016/j.jamda.2007.05.005.
14. Gitlin LN, Winter L, Dennis MP, Hodgson N, Hauck WW. Targeting and managing behavioral symptoms in individuals with dementia: A randomized trial of a nonpharmacological intervention. *J Am Geriatr Soc.* 2010;58(8):1465-1474. doi:10.1111/j.1532-5415.2010.02971.x.
15. Brodaty H, Green A, Koschera A. Meta-analysis of psychosocial interventions for caregivers of

- people with dementia. *J Am Geriatr Soc.* 2003;51(5):657-664.
<http://www.scopus.com/inward/record.url?eid=2-s2.0-0038070244&partnerID=40&md5=9829060980f9dbb17574a661b40292f2>.
16. Cohen-Mansfield J, Jensen B. Assessment and Treatment Approaches for Behavioral Disturbances Associated With Dementia in the Nursing Home: Self-Reports of Physicians' Practices. *J Am Med Dir Assoc.* 2008;9(6):406-413. doi:10.1016/j.jamda.2008.02.010.
 17. Ishii S, Streim JE, Saliba D. A conceptual framework for rejection of care behaviors: Review of literature and analysis of role of dementia severity. *J Am Med Dir Assoc.* 2012;13(1):11-23. doi:10.1016/j.jamda.2010.11.004.
 18. Patel V, Hope RA. Aggressive behaviour in elderly psychiatric inpatients. *Acta Psychiatr Scand.* 1992;85(2):131-135. <http://www.ncbi.nlm.nih.gov/pubmed/1543038>.
 19. Kunik ME, Snow AL, Davila JA, et al. Causes of aggressive behavior in patients with dementia. *J Clin Psychiatry.* 2010;71(9):1145-1152. doi:10.4088/JCP.08m04703oli.
 20. Zeller A, Hahn S, Needham I, Kok G, Dassen T, Halfens RJG. Aggressive Behavior of Nursing Home Residents Toward Caregivers: A Systematic Literature Review. *Geriatr Nurs (Minneap).* 2009;30(3):174-187. doi:10.1016/j.gerinurse.2008.09.002.
 21. Aarsland D, Cummings JL, Yenner G, Miller B. Relationship of aggressive behavior to other neuropsychiatric symptoms in patients with Alzheimer's disease. *Am J Psychiatry.* 1996;153(2):243-247. doi:10.1176/ajp.153.2.243.
 22. Ryden MB. Aggressive behavior in persons with dementia who live in the community. *Alzheimer Dis Assoc Disord.* 1988;2(4):342-355. <http://www.ncbi.nlm.nih.gov/pubmed/3196468>.
 23. Tsai ACH, Lai T-M. Predicting the need of formal care in Taiwan: Analysis of a national random sample. *Arch Gerontol Geriatr.* 2011;53(3):298-302.
<http://www.scopus.com/inward/record.url?eid=2-s2.0-80051664486&partnerID=40&md5=b493c42e08a70a8cf7fde3b71f155efe>.
 24. Hope T, Keene J, Fairburn C, McShane R, Jacoby R. Behaviour changes in dementia. 2: Are there behavioural syndromes? *Int J Geriatr Psychiatry.* 1997;12(11):1074-1078.
 25. Cohen-Mansfield J, Billig N. Agitated Behaviors in the Elderly: I. A Conceptual Review. *J Am Geriatr Soc.* 1986;34(10):711-721. doi:10.1111/j.1532-5415.1986.tb04302.x.
 26. Haley WE, Brown SL, Levine EG. Family Caregiver Appraisals of Patient Behavioral Disturbance in Senile Dementia. *Clin Gerontol.* 1987;6(4):25-34. doi:10.1300/J018v06n04_04.
 27. Taft L. Conceptual analysis of agitation in the confused elderly. *Arch Psychiatr Nurs.* 1989.
<http://psycnet.apa.org/psycinfo/1990-17721-001>. Accessed March 24, 2017.
 28. WOOD SA, CUMMINGS JL, BARCLAY T, HSU M-A, ALLAHYAR M, SCHNELLE JF. Assessing the impact of neuropsychiatric symptoms on distress in professional caregivers. *Aging*

- Ment Health*. 1999;3(3):241-245. doi:10.1080/13607869956208.
29. Asada T, Kinoshita T, Kakuma T. Analysis of behavioral disturbances among community-dwelling elderly with Alzheimer disease. *Alzheimer Dis*. 2000.
http://journals.lww.com/alzheimerjournal/Abstract/2000/07000/Analysis_of_Behavioral_Disturbances_Among.7.aspx. Accessed March 24, 2017.
 30. Chan DC, Kasper JD, Black BS, Rabins P V. Prevalence and correlates of behavioral and psychiatric symptoms in community-dwelling elders with dementia or mild cognitive impairment: The Memory and Medical Care Study. *Int J Geriatr Psychiatry*. 2003;18(2):174-182.
doi:10.1002/gps.781.
 31. Cohen-Mansfield J, Werner P. Environmental influences on agitation: An integrative summary of an observational study. *Am J Alzheimers Dis Other Dement*. 1995;10(1):32-39.
doi:10.1177/153331759501000108.
 32. Cohen-Mansfield J, Thein K, Marx MS. Predictors of the impact of nonpharmacologic interventions for agitation in nursing home residents with advanced dementia. *J Clin Psychiatry*. 2014;75(7):666-671. doi:10.4088/JCP.13m08649.
 33. Kong EH. Agitation in dementia: Concept clarification. *J Adv Nurs*. 2005;52(5):526-536.
doi:10.1111/j.1365-2648.2005.03613.x.
 34. Cohen-Mansfield J, Marx MS, Rosenthal a S. A description of agitation in a nursing home. *J Gerontol*. 1989;44(3):M77-M84. doi:10.1093/geronj/44.3.M77.
 35. Rosen J, Mulsant B, Wright B. Agitation in Severely Demented Patients. *Ann Clin Psychiatry*. 1992;4(3):207-215. doi:10.3109/10401239209149574.
 36. Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The neuropsychiatric inventory. *Neurology*. 1994;44(December):2308-2314.
 37. Jeon Y-H, Sansoni J, Low L-F, et al. Recommended measures for the assessment of behavioral disturbances associated with dementia. *Am J Geriatr Psychiatry*. 2011;19(5):403-415.
doi:10.1097/JGP.0b013e3181ef7a0d.
 38. Volicer L. Behaviors in advanced dementia. *J Am Med Dir Assoc*. 2009;10(2):146; author reply 146-7. doi:10.1016/j.jamda.2008.10.017.
 39. Sloane PD, Rader J, Barrick AL, et al. Bathing persons with dementia. *Gerontologist*. 1995;35(5):672-678.
 40. Sloane PD, Hoeffler B, Mitchell M, et al. Effect of Person-Centered Showering and the Towel Bath on Controlled Trial. *J Am Geriatr Soc*. 2004;52:1795-1804. doi:10.1111/j.1532-5415.2004.52501.x.
 41. Talerico K, Evans L. Making Sense of Aggressive/Protective Behaviors in Persons with Dementia. *Alzheimers care today*. 2000.
http://journals.lww.com/actjournalonline/Abstract/2000/01040/Making_Sense_of_Aggressive_Protective_Behaviors_in.10.aspx. Accessed March 24, 2017.

42. Volicer L. Behaviors in Advanced Dementia. *J Am Med Dir Assoc*. 2009;10(2):146. doi:10.1016/j.jamda.2008.10.017.
43. Farrell Miller M. Physical aggressive resident behavior during hygienic care. *J Gerontol Nurs*. 1997;23(5):24-39. doi:10.3928/0098-9134-19970501-08.
44. Selbæk G, Engedal K. Stability of the factor structure of the Neuropsychiatric Inventory in a 31-month follow-up study of a large sample of nursing-home patients with dementia. *Int Psychogeriatrics*. 2012. http://journals.cambridge.org/article_S104161021100086X. Accessed March 24, 2017.
45. Aalten P, Vugt ME De, Jaspers N, Jolles J, Verhey FRJ. The course of neuropsychiatric symptoms in dementia. Part II : relationship among behavioural sub-syndromes and the influence of clinical variables. *Int J Geriatr Psychiatry*. 2005;20(January):531-536.
46. Cerejeira J, Lagarto L, Mukaetova-Ladinska EB. Behavioral and psychological symptoms of dementia. *Front Neurol*. 2012;MAY(May):1-22. doi:10.3389/fneur.2012.00073.
47. Cummings J, Mintzer J, Brodaty H, et al. Agitation in cognitive disorders: International Psychogeriatric Association provisional consensus clinical and research definition. *Int Psychogeriatr*. 2015:1-11. doi:10.1017/S1041610214001963.
48. B. W, H. B, S. G, et al. Pharmacotherapy of Alzheimer's disease: Is there a need to redefine treatment success? *Int J Geriatr Psychiatry*. 2001;16(7):653-666. <http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L32754925>.
49. Lyketsos CG, Steele C, Galik E, et al. Physical aggression in dementia patients and its relationship to depression. *Am J Psychiatry*. 1999;156(1):66-71. doi:10.1176/ajp.156.1.66.
50. de Medeiros K, Robert P, Gauthier S, et al. The Neuropsychiatric Inventory-Clinician rating scale (NPI-C): reliability and validity of a revised assessment of neuropsychiatric symptoms in dementia. *Int Psychogeriatr*. 2010;22(6):984-994. doi:10.1017/S1041610210000876.
51. Teel CS, Press AN, Lindgren CL, Nichols EG, Teel CS, Press AN. Fatigue among Elders in Caregiving and Noncaregiving Roles. *West J Nurs Res*. 1999;21(4):498-520. doi:10.1177/01939459922044009.
52. Shanks-McElroy HA, Strobino J. Male caregivers of spouses with Alzheimer's disease: Risk factors and health status. *Am J Alzheimers Dis Other Demen*. 2001;16(3):167-175. doi:10.1177/153331750101600308.
53. Esterling BA, Kiecolt-Glaser JK, Glaser R. Psychosocial modulation of cytokine-induced natural killer cell activity in older adults. *Psychosom Med*. 1996;58(3):264-272.
54. Schulz R, Beach SR. Caregiving as a Risk Factor for Mortality. *JAMA*. 1999;282(23):2215. doi:10.1001/jama.282.23.2215.
55. Hooker K, Monahan DJ, Bowman SR, Frazier LD, Shifren K. Personality Counts for a Lot: Predictors of Mental and Physical Health of Spouse Caregivers in Two Disease Groups. *Journals Gerontol Ser B Psychol Sci Soc Sci*. 1998;53B(2):P73-P85. doi:10.1093/geronb/53B.2.P73.

56. Rabins P V., Mace NL, Lucas MJ. The impact of dementia on the family. *Jama*. 1982;248(3):333-335. doi:10.1001/jama.1982.03330030039022.
57. Ornstein K, Gaugler JE. The problem with “problem behaviors”: a systematic review of the association between individual patient behavioral and psychological symptoms and caregiver depression and burden within the dementia patient–caregiver dyad. *Int Psychogeriatrics*. 2012;24(10):1536-1552. doi:10.1017/S1041610212000737.
58. Gaugler JE, Davey a, Pearlin LI, Zarit SH. Modeling caregiver adaptation over time: the longitudinal impact of behavior problems. *Psychol Aging*. 2000;15(3):437-450. doi:10.1037/0882-7974.15.3.437.
59. Gaugler JE, Yu F, Krichbaum K, Wyman JF. Predictors of Nursing Home Admission for Persons with Dementia. *Med Care*. 2009;47(2):191-198. doi:10.1097/MLR.0b013e31818457ce.
60. Pinquart M, Sörensen S. Differences between caregivers and noncaregivers in psychological health and physical health: A meta-analysis. *Psychol Aging*. 2003;18(2):250-267. doi:10.1037/0882-7974.18.2.250.
61. Regier NG, Gitlin LN. Towards defining restlessness in individuals with dementia. *Aging Ment Health*. January 2016:1-10. doi:10.1080/13607863.2015.1128880.
62. Finkel SI. Research Methodologic Issues in Evaluating Behavioral Disturbances of Dementia. *Int Psychogeriatrics*. 1997;8(S2):149-150. doi:10.1017/S104161029700330X.
63. Cheng S-T, Kwok T, Lam LCW. Neuropsychiatric symptom clusters of Alzheimer’s disease in Hong Kong Chinese: Prevalence and confirmatory factor analysis of the Neuropsychiatric Inventory. *Int Psychogeriatrics*. 2012;24(9):1465-1473. doi:10.1017/S1041610212000609.
64. Nowrangi M a, Lyketsos CG, Rosenberg PB. Principles and management of neuropsychiatric symptoms in Alzheimer’s dementia. *Alzheimers Res Ther*. 2015;7. doi:10.1186/s13195-015-0096-3.
65. Lyketsos CG. Neuropsychiatric symptoms (behavioral and psychological symptoms of dementia) and the development of dementia treatments. *Int Psychogeriatr*. 2007;19(3):409-420. doi:10.1017/S104161020700484X.
66. Kales HC, Gitlin LN, Lyketsos CG. Assessment and management of behavioral and psychological symptoms of dementia. *BMJ*. 2015;350:h369. doi:10.1136/bmj.h369.
67. Pearlin LI, Mullan JT, Semple SJ, Skaff MM. Caregiving and the stress process: an overview of concepts and their measures. *Gerontologist*. 1990;30(5):583-594. doi:10.1093/geront/30.5.583.
68. Mesulam M-M. Some cholinergic themes related to Alzheimer’s disease: Synaptology of the nucleus basalis, location of m2 receptors, interactions with amyloid metabolism, and perturbations of cortical plasticity. *J Physiol*. 1998;92(3-4):293-298. doi:10.1016/S0928-4257(98)80036-3.
69. Stewart JT, Gonzalez-Perez E, Zhu Y, Robinson BE. Cognitive predictors of resistiveness in dementia patients. *Am J Geriatr Psychiatry*. 1999;7(3):259-263.
70. Hodgson NA, Gitlin LN, Winter L, Czekanski K. Undiagnosed illness and neuropsychiatric

- behaviors in community residing older adults with dementia. *Alzheimer Dis Assoc Disord*. 2011;25(2):109-115. <http://www.scopus.com/inward/record.url?eid=2-s2.0-79958282325&partnerID=40&md5=0a8d11f39f29f35c22e10532dcc2c6c1>.
71. von Gunten A, Pocnet C, Rossier J. The impact of personality characteristics on the clinical expression in neurodegenerative disorders—A review. *Brain Res Bull*. 2009;80(4-5):179-191. doi:10.1016/j.brainresbull.2009.07.004.
 72. Hoeffler B, Rader J, McKenzie D, Lavelle M, Stewart B. Reducing aggressive behavior during bathing cognitively impaired nursing home residents. *J Gerontol Nurs*. 1997;23(5):16-23.
 73. Williams KN, Herman R, Gajewski B, Wilson K. Elderspeak communication: impact on dementia care. *Am J Alzheimers Dis Other Dement*. 2009;24(1):11-20. doi:10.1177/1533317508318472.
 74. Hall GR, Buckwalter KC. Progressively lowered stress threshold: A conceptual model for care of adults with Alzheimer's disease. *Arch Psychiatr Nurs*. 1987;1(6):399-406.
 75. L.N. G, L. W, M.P. D, N. H, W.W. H. Targeting and managing behavioral symptoms in individuals with dementia: A randomized trial of a nonpharmacological intervention. *J Am Geriatr Soc*. 2010;58(8):1465-1474. <http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L359292126>.
 76. Aneshensel CS, Pearlin LI, Mullan JT, Zarit SH, Whitlatch CJ. *Profiles in Caregiving: The Unexpected Career*. Academic Press; 1995.
 77. Son J, Erno A, Shea DG, Femia EE, Zarit SH, Stephens MAP. The caregiver stress process and health outcomes. *J Aging Health*. 2007;19(6):871-887.
 78. Ornstein K, Gaugler JE, Devanand DP, Scarmeas N, Zhu C, Stern Y. The differential impact of unique behavioral and psychological symptoms for the dementia caregiver: How and why do patients' individual symptom clusters impact caregiver depressive symptoms? *Am J Geriatr Psychiatry*. 2013;21(12):1277-1286. doi:10.1016/j.jagp.2013.01.062.
 79. Hooker K, Bowman SR, Coehlo DP, et al. Behavioral change in persons with dementia: relationships with mental and physical health of caregivers. *J Gerontol B Psychol Sci Soc Sci*. 2002;57(5):P453-P460. doi:10.1093/geronb/57.5.P453.
 80. Langa KM, Larson EB, Crimmins EM, et al. A Comparison of the Prevalence of Dementia in the United States in 2000 and 2012. *JAMA Intern Med*. 2017;177(1):51. doi:10.1001/jamainternmed.2016.6807.
 81. Schulz R, Martire LM. Family Caregiving of Persons With Dementia: Prevalence, Health Effects, and Support Strategies. *Am J Geriatr Psychiatry*. 2004;12(3):240-249. doi:10.1097/00019442-200405000-00002.
 82. Steinberg M, Tschanz JT, Corcoran C, et al. The persistence of neuropsychiatric symptoms in dementia: the Cache County Study. *Int J Geriatr Psychiatry*. 2004;19(1):19-26. doi:10.1002/gps.1025.
 83. De Vugt ME, Stevens F, Aalten P, et al. Do caregiver management strategies influence patient behaviour in dementia? *Int J Geriatr Psychiatry*. 2004;19(1):85-92. doi:10.1002/gps.1044.

84. Okura T, Langa KM. Caregiver burden and neuropsychiatric symptoms in older adults with cognitive impairment: the Aging, Demographics, and Memory Study (ADAMS). *Alzheimer Dis Assoc Disord*. 2011;25(2):116-121. doi:10.1097/WAD.0b013e318203f208.
85. Beeri MS, Werner P, Davidson M, Noy S. The cost of behavioral and psychological symptoms of dementia (BPSD) in community dwelling Alzheimer's disease patients. *Int J Geriatr Psychiatry*. 2002;17(5):403-408. doi:10.1002/gps.490.
86. Rabins P V., Black BS. Measuring quality of life in dementia: purposes, goals, challenges and progress. *Int Psychogeriatrics*. 2007;19(3):401. doi:10.1017/S1041610207004863.
87. Wancata J, Windhaber J, Krautgartner M, Alexandrowicz R. The Consequences of Non-Cognitive Symptoms of Dementia in Medical Hospital Departments. *Int J Psychiatry Med*. 2003;33(3):257-271. doi:10.2190/ABXK-FMWG-98YP-D1CU.
88. Mahoney EK, Trudeau S a, Penysack SE, MacLeod CE. Challenges to intervention implementation: lessons learned in the Bathing Persons with Alzheimer's Disease at Home study. *Nurs Res*. 2006;55(2 Suppl):S10-S16. doi:10.1097/00006199-200603001-00003.
89. Huang H-L, Shyu Y-IL, Chen S-T, Hsu W-C. Caregiver self-efficacy for managing behavioural problems of older people with dementia in Taiwan correlates with care receivers' behavioural problems. *J Clin Nurs*. 2009;18(18):2588-2595. doi:10.1111/j.1365-2702.2008.02547.x.
90. Åström S, Bucht G, Eisemann M, Norberg A, Saveman BI. Incidence of violence towards staff caring for the elderly. *Scand J Caring Sci*. 2002;16(1):66-72. doi:10.1046/j.1471-6712.2002.00052.x.
91. Alzheimer's Association. 2015 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2015;11(3):332-384. <http://www.ncbi.nlm.nih.gov/pubmed/25984581>. Accessed March 24, 2017.
92. Baumgarten M, Battista RN, Infante-Rivard C, Hanley JA, Becker R, Gauthier S. The psychological and physical health of family members caring for an elderly person with dementia. *J Clin Epidemiol*. 1992;45(1):61-70. doi:10.1016/0895-4356(92)90189-T.
93. Murray J, Schneider J, Banerjee S, Mann A. EURO CARE: a cross-national study of co-resident spouse carers for people with Alzheimer's disease: II—a qualitative analysis of the experience of caregiving. *Int J Geriatr Psychiatry*. 1999;14(8):662-667. doi:10.1002/(SICI)1099-1166(199908)14:8<662::AID-GPS993>3.0.CO;2-4.
94. Mahoney EK, Hurley AC, Volicer L, et al. Development and testing of the resistiveness to care scale. *Res Nurs Heal*. 1999;22(1):27-38. doi:10.1002/(SICI)1098-240X(199902)22:1<27::AID-NUR4>3.0.CO;2-T.
95. Hurley A, Volicer L, Camberg L. Measurement of observed agitation in patients with dementia of the Alzheimer type. *J Ment*. 1999.
96. Cohen-Mansfield J, Marx MS, Dakheel-Ali M, Regier NG, Thein K, Freedman L. Can agitated behavior of nursing home residents with dementia be prevented with the use of standardized stimuli? *J Am Geriatr Soc*. 2010;58(8):1459-1464. doi:10.1111/j.1532-5415.2010.02951.x.
97. Gitlin LN, Winter L, Dennis MP, Hodgson N, Hauck WW. A biobehavioral home-based

intervention and the well-being of patients with dementia and their caregivers: the COPE randomized trial. *JAMA*. 2010;304(9):983-991. doi:10.1001/jama.2010.1253.

98. Ishii S, Streim JE, Saliba D. A conceptual framework for rejection of care behaviors: Review of literature and analysis of role of dementia severity. *J Am Med Dir Assoc*. 2012;13(1):11-23. doi:10.1016/j.jamda.2010.11.004.

CHAPTER 2: MANUSCRIPT 1

Rejection of care, Aggression, and Agitation in Persons with Dementia: A Systematic Review of Definitions Used in Behavioral and Psychological Symptoms of Dementia Measures

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ABSTRACT

Objective: To provide a systematic review of how rejection of care, aggression, and agitation are described and operationalized in existing measures of dementia-related behaviors with a particular focus on whether these behaviors are conceptualized as separate phenomena in rating scales.

Methods: We reviewed two systematic reviews of behavioral measures in dementia to evaluate their definitions and operationalization of rejection, aggression, and agitation. Additionally, we conducted a systematic review of English-language peer-reviewed articles published from 1980 to 2017 to update the previous list instruments and identify additional measures that were not captured in previous reviews.

Results: 43 instruments (23 general behavior measures, 20 symptom-specific measures) developed to measure behavioral symptoms were included. Of these, 25 (58.1%) included items related to rejection of care; 32 (74.4%) included aggression items; and 35 (81.4%) had agitation items. Descriptions and definitions of the behaviors were highly variable across instruments. 13 of 23 general measures and 3 of 20 symptom specific measures included items separately representing all three behaviors while the rest of the measures lacked items measuring one or two behaviors of our interest.

Conclusions: The review demonstrated that rejection, aggression, and agitation are measured in most scales yet their measurement is highly variable and they are often not distinguished from each other. Researchers and clinicians need to consider each symptom in its own right and revise existing instruments to address possible misnomers to improve measurement of dementia behaviors.

INTRODUCTION

Dementia is a growing public health problem. As the segment of the U.S. population age 65 and older increases rapidly, so too will the numbers of people with dementia. The number of older adults with dementia in the U.S. is projected to nearly triple from 5.1 million in 2015 to 13.8 million in 2050 (Alzheimer's Association, 2016; Callahan et al., 2012).

Along with cognitive and functional declines, behavioral symptoms (e.g., agitation, wandering) are the hallmark of dementia. Nearly all individuals with dementia will exhibit one or more behavioral symptoms over the course of the illness (Steinberg, 2004). These symptoms have been associated with significant distress for caregivers as well as for persons with dementia (de Vugt, 2004; Okura, 2011), early nursing home placement (Chan, 2003), increase in health care costs (Schneider, 2002), faster disease progression (Rabins, 2011), and increased risks for morbidity and mortality (Wancata, 2003).

As we know about behaviors in people with dementia through how they are measured, the purpose of this paper is to provide a systematic review of how rejection of care, aggression, and agitation are described and operationalized with a particular focus on whether these behaviors are conceptualized as separate phenomena in rating scales. As measurement drives our understanding of prevalence and how these behaviors are characterized, a review of this nature is critical because it may assist clinicians and researchers to choose the optimal instruments for their study purpose and characteristics of their study population. It may also serve as a guide for clinicians and researchers developing new or enhanced instruments that can detect or track changes in dementia-related behaviors more precisely.

Behavioral symptoms often occur in clusters that are not well delineated and their occurrences may overlap with each other. One of the most frequently occurring and fairly consistently delineated behavioral types is agitation. Agitation-type behaviors is a broad category that may include a wide range of behaviors (e.g., restlessness, pacing, repetitive questioning). Agitation has been defined differently depending upon its measurement. The Cohen-Mansfield Agitation Inventory, one of the first and is the most widely used instruments to measure agitated-type behavioral symptoms in dementia, defines

agitation as ‘inappropriate verbal, vocal, or motor activity that is not judged by an outside observer to result directly from the needs or confusion of the agitated individual.’ (Cohen-Mansfield, 1989). It is concerning, however, that in most measures, the definition of agitation is broad and appears to encompass distinct behavioral manifestations.

Two behaviors typically subsumed under agitation and frequently observed as co-occurring are rejection of care and aggression. Each of these behaviors may be a distinct a group of behaviors. Rejection of care has been defined as the ‘repertoire of behaviors with which persons with dementia withstand or oppose the efforts of a caregiver.’ (Mahoney, 1999) Rejection of care behaviors may include screaming, hitting, and/or kicking that occur during the act of helping with self-care or activities of daily living (ADL). Rejection of care can manifest itself as an aggressive form of behavior occurring in the context of caregiving (Mahoney, 1999) and thus its distinction with aggression can be blurred. Aggression, on the other hand, has been defined an ‘overt act, involving the delivery of noxious stimuli to (but not necessarily aimed at) another object, organism or self, which is clearly not accidental (Patel, 1992).’ Aggression covers a range of different behaviors, some of which overlap with agitation or rejection of care.

The conceptual distinction among these three behaviors has not been clearly delineated and has been confounded by measures which either group them under one rubric or do not fully explicate one from the other. There have been only a few previous attempts to distinguish these behaviors. For example, Hurley et al. (1999) argued that the term ‘agitation’ should be reserved for behaviors that occur when a person with dementia is alone and any inappropriate behaviors that occur within the context of caregiving should be named ‘rejection of care’. Ishii et al. (2012) differentiated rejection of care and aggression based on the intent of the person with dementia. According to these authors only the behaviors with the underlying intent to harm others are aggression, and self-defensive behaviors should be rejection of care. Furthermore, the majority (98%) of 557 psychogeriatric clinicians who responded to a survey asking about the definition of agitation reported that agitation and aggression may be overlapping but not the same behavior (Cummings, 2015).

A recent review evaluated definitions of behavioral symptoms in 14 instruments developed to measure the behavioral and psychological symptoms of dementia (BPSD) with a particular focus on their ability to separate agitation from aggression (Volicer, 2017). This review also noted a confused nomenclature of behavioral symptoms and proposed that the outcomes should be evaluated separately for agitation and aggression in treatment studies of behavioral symptoms of dementia. However, this was not an exhaustive review of all available measurement scales and did not examine rejection of care as a concept that needed to be differentiated from agitation or aggression.

It is important to distinguish rejection of care, aggression, and agitation because their underlying etiologies and hence management strategies can be quite different. Confusing terminology used in measurement scales prevents clinicians and researchers from being able to assess which behavioral symptoms are responsive to a pharmacological or nonpharmacological intervention. Porsteinsson (2014) evaluated the efficacy of an antidepressant for the treatment of agitation in persons with dementia, and reported that the drug was effective in managing agitation on the CMAI but not on NPI agitation subscale. In fact descriptions of agitation in these two scales are very different and they may possibly measure two different concepts of behavior.

This review is the first to our knowledge to examine whether existing instruments contain items representing rejection of care, aggression, and agitation. Our aim was to review existing measures of dementia-related behaviors for items specific to each of the three symptoms of our interest. Further, we set out to examine how these behaviors are described and defined in question wording of identified items and whether the behaviors are separately operationalized or lumped together within an item or a category.

In many studies, these behaviors were not clearly defined and/or differentiated from each other. Lack of a consensus as to where the boundaries of these behaviors lie often resulted in a considerable or sometimes complete overlap among these behaviors in their characterization or operationalization. For the purpose of this review, we have used the criterion proposed by Hurley, 1999 that distinguished rejection of care and agitation on the basis of whether behaviors occur during an interaction between the person with dementia and the caregiver. That is, only the behaviors that occur when the person with dementia is

solitary (e.g., restlessness, repetitive movements, crying out) are categorized as agitation while the same behaviors, when occurring within the context of caregiving, should be considered rejection of care. Similarly, agitation was differentiated from aggression on the basis of a contextually oriented typology proposed by Volicer et al., 2017, which separates behaviors *directed toward others* (aggression) and behaviors *not directed toward others* (agitation). This framework for differentiating behaviors, however, may not correspond to labeling or categorization of behaviors provided by the authors of the instruments. The intent was to obtain non-overlapping groups of items for each behavioral symptom without relying on instrument inventors' conceptualization of these behaviors. Research questions were: Are rejection of care, aggression, and agitation measured separately (i.e., as different items or subdomains) in dementia behavior scales? How are these behaviors described and categorized in dementia behavior scales?

METHODS

Search procedure

To evaluate measures for their definition and operationalization of the 3 behaviors of interest, two systematic reviews of behavioral measures were used and an additional literature review to capture new measures between 2014 and 2017 were conducted. The first review conducted by Gitlin et al. (2014) examined existing, psychometrically sound measures of BPSD. In this exhaustive review, they included all identified scales available in English that had been developed and/or tested with dementia populations and had adequate psychometric properties. Additionally, a list of most commonly used BPSD instruments from another review (van Derlinde, 2014) was reviewed for inclusion. To update this list of instruments and identify additional measures with psychometric properties, a separate comprehensive computerized search of peer-reviewed articles (January 1980 – February 2017) was also conducted in PubMed, CINAHL Plus, and PsycINFO using the following search terms: *neuropsychological test*, *neuropsychological measurements*, *dementia*, *Alzheimer's disease*, *behavior*, *delusions*, *hallucinations*, *agitation*, *depression*, *anxiety*, *eating*, *euphoria*, *apathy*, *disinhibition*, *irritability*, *motor disturbance*, *sleep*, *vocalizations*, *assaultive behavior*, *aggression*, *problem behavior*,

psychomotor agitation, rejection of care, resistiveness of care, resistance to care, uncooperative behavior, and obstreperous behavior. Two authors (SC and MC) independently reviewed all titles and abstracts of papers to select measures that meet the following criteria: (a) published in English; (b) developed for or tested in people with dementia; (c) included items measuring rejection of care, aggression, or agitation; and (d) one or more psychometric properties were reported. The authors then reviewed the wording of the selected instruments for its relevance to rejection of care, aggression, and agitation.

RESULTS

45 articles from Gitlin et al., 2014 and 32 articles from van Derlinde et al., 2014 were reviewed (Figure 1). After removing 14 duplicates, 25 with no measure of behavioral symptoms, and 4 inaccessible instruments, 38 were retained. Additionally, a computerized search yielded 4,341 papers. The abstracts of 312 relevant studies were screened and cross-checked with previously identified papers, which resulted in only 1 additional paper that met our inclusion criteria. After adding 4 articles from manual searches, we have identified a total of 43 scales that are used to measure behavioral symptoms (Table 2).

Characteristics of instruments

Table 1 shows the characteristics of the identified instruments for measuring behavioral symptoms of dementia. Of the 43 instruments, 23 (53.5%) measure multiple behavioral symptoms in persons with dementia whereas 20 (46.5%) target a particular behavioral or psychological domain. Symptom-specific measures were identified for 8 behavioral domains: agitation (n=6, 30.0%; Logsdon; Finkel; Cohen-Mansfield; Yudofsky; Rosen; Hurley), aggression (n=5, 25.0%; Perlman; Yudofsky; Patel; Ryden; Palmstierna), depression (n=3, 15.5%; Alexopoulos; Yesavage; Hamilton), wandering (n=2, 10.0%; Algate; Algate), anxiety (n=1, 5.0%; Shankar), disruptive vocalization (n=1, 5.0%; Burgio), rejection of care (n=1, 5.0%; Mahoney), and sleep disorders (n=1, 5.0%; Tractenberg).

Items on instruments describing rejection of care, aggression, and agitation are displayed in Table 2. The number of items was highly variable across the instruments. For general measures, the number of

items ranged from 10 to 142, with most scales allotting one to three items to each behavior. For symptom-specific instruments, the number of items ranged from 1 to 30. Measures also varied widely as to the time frames used in questionnaires, which ranged from the current time (mainly used for observational measures), to past days, weeks or year. As for the setting of the scales, 12 measures were designed for use in skilled nursing facilities, 8 for use in the hospital setting, 8 for unspecified settings, 5 for use in the community and skilled nursing facility settings, 5 for use in community-based settings, 4 for use in the hospital and skilled nursing facility settings, and 1 for use in the community and hospital settings.

Rejection of care

Rejection of care was measured by 25 of 43 (58.1%) instruments. The number of items measuring rejection of care in each scale ranged from 1 to 13 with most instruments relying on a single item to identify rejection of care. Rejection of care was described variably in these instruments. The term ‘uncooperativeness’ was used in 9 (36.0%) instruments out of 25 that included at least one rejection of care item, followed by ‘resisting care / resistance to care’ (n=8, 32.0%), ‘refusing care’ (n=5, 20.0%), ‘stubbornness’ (n=4, 16.0%), ‘noncompliance’, ‘refusing or spitting medications’, and ‘leaving table during meals’ (all n=2, 8.0%) (Table 3). In two scales (Reisberg; Auer), the term ‘agitation’ was used to describe rejection of care. The description of ‘agitation’ in these scales stated ‘refusal to bathe, dress, continue walking, take medications’ (Reisberg) and ‘does not want to be helped, or other refusals indicative of negativity’, and therefore these items were considered rejection of care in this review. Also, one study (Mahoney) which was specifically developed to characterize and quantify rejection of care included 13 challenging behaviors related to rejection of care (e.g., hitting/kicking, grabbing, screaming) that can occur during ADL care.

We have also investigated domain names where rejection of care items were categorized. Of the 25 scales that included rejection of care items, 14 had no categories or domains. Of the 11 with subdomains, rejection of care was categorized under ‘aggression’ in 4 studies, ‘agitation/aggression’ in 2

studies, and ‘disturbing behavior’, ‘irritability’, ‘agitation’, and ‘other clinical features’ all respectively in one study.

Aggression

Aggression was measured in 32 of 43 measures (74.4%) instruments, of which 21 were general measures and 11 were symptom-specific measures including 5 specifically developed to measure aggressive behaviors. The number of items used to identify aggressive behaviors ranged from 1 to 20 with the total of 126.

Of the 21 general measures, 6 studies used a single item, which did not specify types of aggression, to measure aggressive behaviors: ‘hostility’ (n=4), ‘becoming angry and threatening’ (n=1), and ‘verbal or physical aggression’ (n=1). 10 instruments used two items to measure aggression which separated ‘verbal aggression’ and ‘physical aggression’ but without specifying subtypes (Table 3). 6 studies included more than two items measuring various types of verbal and/or physical aggression. The descriptions of aggressive behaviors fell into 4 main categories: verbal aggression, physical aggression, destruction of property, and self-harm. The types of verbal aggression described in these scales encompassed a wide range of specific behaviors including ‘cursing’, ‘swearing’, ‘yelling’, ‘shouting’, ‘screaming’, and ‘hostile/accusatory language’ while the types of physical aggression included ‘hitting’, ‘kicking’, ‘biting’, ‘scratching’, ‘pushing’, ‘grabbing’, ‘fighting’, and ‘using a weapon.’ The other aggressive types, ‘destroying property’ and ‘self-harm’ were used in 8 and 4 measures respectively.

Of the 11 symptom-specific measures that included aggression items, 5 were aggression measures while 6 were developed to measure other dementia symptoms. These scales tend to have more questions to measure aggression than general measures do, with the number of items ranging from 2 to 20. The majority of the agitation scales (n=5, 83.3%) included aggression items, and one observation scale for ‘disruptive vocalization’ included items that could be described as verbal aggression (‘screaming’, ‘cursing’). Symptom-specific scales for anxiety, depression, rejection of care, sleep disorders, and wandering had no aggression items. Physical and verbal aggression were measured in 10 of the 11

symptom-specific scales which included aggression items. Questions describing ‘destroying property’ and ‘self-harm’ were included in 8 and 3 scales respectively.

As for domain names for aggression, 12 rating scales had aggression items in one or more subdomains, of which 7 studies categorized aggression items under ‘aggression’ (n=5) or ‘aggression/agitation’ domain (n=2). Other domain names under which aggression was classified included ‘disinhibition’, ‘behavioral disturbances’, ‘irritability’, ‘dangerous behavior’, ‘disturbing behavior’, ‘aberrant vocalization’, ‘vocalizations and oral/facial movements’, and ‘upper and/or lower extremity movements’.

Agitation

35 (81.4%) of the 43 scales included items measuring agitated-type behaviors. The number of agitation items in each scale ranged from 1 to 12 with the total number for all scales being 122. Descriptors of agitation were highly variable across instruments with ‘wandering’ used in 20 (57.1%) instruments, ‘repetitive activities or movements’ in 17 (48.6%), ‘pacing’ in 16 (45.7%), ‘restlessness or fidgeting’ in 15 (42.9%), ‘noise making or screaming (not directed toward others)’ in 13 (37.1%), ‘agitation’ in 12 (34.3%), ‘increased motor activity or motor hyperactivity’ in 8 (22.9%), ‘attention seeking behavior’ in 6 (17.1%), and ‘excessive talking’ in 2 (5.7%) (Table 3).

Domain names in which agitated behaviors were included were also highly heterogeneous. ‘Behavioral disturbances’ (or ‘activity disturbances’, ‘motor disturbance’, ‘aberrant motor behavior’) was used in 8 scales representing the only domain name that was used more than two scales. Other domain names for agitation were ‘disinhibition’, ‘sundowning’, ‘social disruptiveness’, ‘restlessness’, ‘irrational or restless behavior’, ‘annoying behavior’, ‘inappropriate behavior’, ‘aberrant vocalization’, ‘agitation’, ‘vocalizations and oral/facial movements’, ‘upper and lower extremity movements’, and ‘other clinical features’.

Separation of behaviors on instruments

As shown in Table 4, 13 of 23 (56.5%) general measures included separate items representing all three behaviors. The rest of the general measures (43.5%) did not include one of the three behaviors with rejection of care being the most frequently unmeasured behavior. 8 of 20 (40.0%) symptom specific measures included items relevant to only one symptom, which is mostly what the measure is designed to capture. For example, Ryden Aggression Scale does not include either rejection of care or agitation items. However, 3 symptom specific scales developed to measure agitation (i.e., ABID, CMAI, PAS) included items representing all of the three behaviors.

Confusion of construct categorization

Apart from the use of varying terms to describe these behaviors, categorization of these behaviors in studies has been inconsistent and sometimes contradictory. This confusion of labeling and categorization was best illustrated in two of the most widely used and most recommended dementia-related tools for clinicians and researchers (Jeon, 2011; Bentvelzen, 2017). In BEHAVE-AD (Reisberg) the item ‘agitation’ is described as *“negativity including refusal to bathe, dress, continue walking, take medications.”* which mainly indicates rejection of care. And this item is categorized under ‘aggression’ domain. Also, the NPI (Cummings) uses a screening question for a domain which combines ‘agitation’ and ‘aggression’ into one category (‘agitation/aggression’), that clearly asks if a person with dementia rejects care while interacting with a caregiver (*“Does the patient have periods when he/she refuses to cooperate or won’t let people help him/her? Is he/she hard to handle?”*). Since this is a screening question, a respondent with a negative response will never be asked follow-up questions about specific behaviors within the domain. Further, an abbreviated version of the NPI (NPI-Q) which does not contain any screening questions includes only one survey question for ‘agitation/aggression’ domain (*“Is the patient resistive to help from others at times, or hard to handle?”*) which corresponds to our definition of rejection of care. Since there is only one question for each of the 12 domains in NPI-Q, this question is thought to reflect what the authors think cardinal symptoms of ‘agitation/aggression’ domain are.

Identification of symptom groups

We have examined the studies that reported factor solutions of their items in order to identify symptom grouping of rejection of care, aggression, and agitation and to investigate whether symptom groups identified in the literature support our distinction among the three behaviors. However, due to considerable heterogeneity in symptom/domain names, definitions, group inclusions, and factor loadings across the studies, it was virtually impossible to compare study results and derive consistent factor solutions.

DISCUSSIONS

Despite persistent confusion in the definitions and features differentiating behavioral symptom groups, study of agitation and its distinction from relevant behaviors has not received much research attention. Distinguishing among rejection of care, aggression, and agitation is essential in formulating treatment strategies for persons with dementia because these three behaviors may have different contextual etiologies, warranting different treatment approaches. Also, as this review shows, each of these result in distinct, observable behaviors that can be measured. For example, verbal agitation resulting from boredom can be alleviated by providing persons with dementia with social stimuli (Cohen-Mansfield, 2010), while verbal agitation during caregiving activities (hence rejection of care) may be managed by better caregiver communication (e.g., explain every step of care to person with dementia slowly in simple sentences). Similarly, aggressive behaviors, which may follow a rejection of care episode or be encompassed in rejecting behavior (Bridges-Parlet, 1994), may be prevented by recognizing rejection of care and keeping the behavior from escalating into combative behaviors (Kunik, 2010).

Although there has been recent empirical evidence supporting delineation of these behaviors (Choi, 2017; de Medeiros, 2010; Volicer, 2007; Mahoney, 1999), traditionally in dementia behavior scales the boundaries of these behaviors have been unclear and in some cases these behaviors were not even recognized as clinical constructs. The current systematic review demonstrates the lack of boundaries as it concerns these behaviors. This is particularly the case in the use of differing labels for the same type

of behavior which gives rise to confusion regarding the definitions and conceptualizations of these three behaviors. Given that the instruments that cause most confusion in labeling these behaviors are the ones that are often considered a gold standard for measuring behaviors in persons with dementia, there is a danger that this confusion of the behavioral symptom terminology may be perpetuated.

The examination of the literature also reveals that domain classification of these behaviors is highly variable. Of the 25 instruments that included rejection of care items, 11 contained subdomains, of which no domain was named rejection of care, indicating authors' lack of acknowledgement of rejection of care as an independent behavioral domain. With regard to aggression, 7 of the 12 instruments which included any aggression item had one or more aggression items under 'aggression' domain. Some of these scales used multidomains to categorize aggression items however. For example, NPI-C has aggression items in two different domains (i.e., 'aggression' and 'aberrant vocalizations'). As for agitation, besides 6 symptom-specific scales designed to measure agitation, the term 'agitation' was rarely used as a domain name in general measures. Only 1 study (Cummings) of the 13 instruments which included agitation items had an 'agitation' domain. Authors appear to conceptualize physical/motor activities more as agitation than other types of behavior (e.g., verbal symptoms). This was demonstrated by the fact that of the 20 domains under which agitation items were classified, 8 had domain names such as 'motor disturbance' or 'behavioral disturbances' while the rest domains were so heterogeneous that no one domain name was used in more than two studies. Lack of consensus definition as well as non-specific and multidimensional nature of agitation (Cummings; Kong) may have contributed to this heterogeneity, which would make combining tools across domains to develop a common framework nearly impossible. Of note is that agitation items were also used in other instruments particularly designed to measure psychological symptoms such as anxiety and depression, blurring its boundaries with psychiatric diagnoses such as mood disorders.

Another point of confusion in terminology identified by this review is the double labeling of the items that may have overlapping features but are not necessarily the same behavior. 'Pacing / wandering' was used in 6 studies while 'restlessness / agitation' in 4 studies. These behaviors have not been well

defined in the literature, and some researchers argue that these are different behaviors that need to be identified distinct (Regier, 2017; Algase, 2008). Further, in two studies, behaviors that should belong to two very different domains were combined together to form a single item: ‘hostility/uncooperativeness’ (Levein, 1987_NRS) and ‘uncooperative or aggressive behavior’ (Ray, 1992). Traditionally ‘hostility’ has been considered an intentional offensive behavior, and thus often termed ‘aggression’ (Gates, 2003) while ‘uncooperativeness’, which is a reactive behavior, is the description used to describe ‘rejection of care’ in some behavioral studies. Also, one instrument (CMAI) includes two aggressive behaviors with possibly different intents into one item (‘hurting self or others’). However, these two behaviors may have very different underlying motivations (i.e., suicidal ideation vs. homicidal ideation) and therefore should be measured separately (Wand, 2017). This proposition may be corroborated by the fact that ‘threats to hurt oneself’ item loaded on ‘depression’ factor and not on ‘disruption’ factor in RMBPC.

It is also problematic that most measurement scales regardless as to how these three behaviors are defined, do not provide contextual characteristics in which behaviors occur, and this has affected in turn how we categorize behaviors. For example, as this review shows, in most cases aggressive behaviors are measured using a single item asking about the presence of physical or verbal aggression without further description of the situations in which they may occur. A spitting behavior by a person with dementia could be categorized as ‘aggression’ if it was purposeful and directed toward someone. However, if spitting occurred in a situation such as medication administration or feeding, the behavior should be classified as ‘rejection of care’ according to the definitions used in this review. A decontextualized description of a simple occurrence of observable behavior cannot provide such information. Additionally, information as to whether a behavior is directed toward someone and whether a behavior is intentional, although intent is difficult to assess, will provide valuable insight into distinction between ‘agitation’ and ‘aggression’.

Based on this review, we propose that dementia behavior rating scales should include items representing rejection of care, aggression, and agitation and that outcomes should be measured separately for these behaviors. This is important for clinical trials testing effectiveness of a pharmacological and/or

nonpharmacological interventions since the intervention may be differentially effective on these symptoms (Porsteinsson, 2014; Volicer, 2017).

To be able to do this, researchers should begin to recognize rejection of care as a separate symptom from aggression and/or agitation. Our results showed that 42% of the instruments reviewed did not have any item related to rejection of care. This is concerning given that there is evidence that rejection of care may be a modifiable risk factor for aggressive behaviors in persons with dementia (Volicer, 2009).

Choi et al. (2017) recategorized the items of the Agitated Behavior In Dementia scale to create unique combinations of rejection of care, aggression, and agitation and reported that these clusters of behaviors had different relationships with important clinical variables in community-dwelling persons with dementia. In this study they used a single item to represent rejection of care, and those caregivers who reported the occurrence of rejection of care in addition to agitation had a different relationship with the level of cognitive impairment of the person with dementia compared to the caregivers who reported the presence of agitation only without rejection of care. This finding suggests that researchers or clinicians using scales that include even a single rejection of care item may be able to find significant associations between unique behavioral symptom clusters and various clinical variables that they otherwise would not be able to find by applying a different categorization scheme. We recommend that future studies should choose an instrument that includes at least one rejection of care item as well as aggression and agitation items and consider recategorizing the items based on the categorization schema that takes into consideration the circumstances of the behavioral symptoms.

Lastly, of the scales that we reviewed, the NPI is by far the most widely used instrument with over 5,000 citations, followed by the BEHAVE-AD with over 200 citations. As discussed earlier, items under ‘agitation/aggression’ in the NPI and ‘agitation’ in the BEHAVE-AD appear to actually measure rejection of care. We propose that these domain/item names be changed to or renamed something that reflects this construct to stop the perpetuation of confusing terminology of these symptoms.

LIMITATIONS

There are several limitations. One limitation of this review is that there are a variety of definitions for rejection of care, aggression, and agitation, and there may be other methods to define and distinguish these behaviors. Although there is empirical evidence supporting a distinction between agitation and rejection of care (Volicer) as well as a distinction between agitation and aggression (de Medeiros), little is known about distinction of all three behaviors. Another limitation is that this review was not an exhaustive account of every single instrument in all possible populations and settings. Also, most instruments are old (i.e., developed over 15 years ago) and are not frequently used. However, level of the impact of a rating scale was not examined in this review and we cannot determine if the definitions used in higher-impact scales are more representative of the conceptualization of dementia behaviors by generations of clinicians and researchers, and should be given preference. Lastly, our searches were limited to studies published in English.

CONCLUSION

This comprehensive review of dementia-related instruments shows that rejection of care, aggression, and agitation are measured in most scales yet their measurement is highly variable and they are often not distinguished from each other. The varying definitions/descriptions and categorization of these behaviors across studies demonstrate the significant confusion and conflation of concepts that exists in the field. Heterogeneity of items that can be included in a definition of agitation makes it very difficult for a boundary to be drawn between agitation and the other two behaviors while lack of consideration for the context in which behaviors occur mostly confounds aggression and rejection of care. A clear conceptual definition, recognition of distinction among symptoms, and availability of congruent measures are an important basis for knowledge development. Better measurements of rejection of care, aggression, and agitation are needed to develop better pharmacological and nonpharmacological treatment strategies. Also, using a common language in measurement scales will facilitate comparability of findings and enhance clinical usefulness of research studies.

Additionally, this literature review revealed that few studies included items describing the situation or context in which behaviors occurred. Description of the context is important in that it helps to distinguish behaviors that require different nonpharmacological management strategies. Fortunately rejection of care items can provide information regarding the circumstances under which behaviors occur. Revision of existing instruments to address possible misnomers as well as development of a new instrument that characterizes the context in which behaviors occur and conceptually differentiates rejection of care, aggression, and agitation is particularly needed to improve measurement of dementia behaviors and devise optimal treatment strategies.

REFERENCES

- Aalten, P., Verhey, F. R., Boziki, M., Bullock, R., Byrne, E. J., Camus, V., ... & Frisoni, G. (2007). Neuropsychiatric syndromes in dementia. *Dementia and geriatric cognitive disorders*, 24(6), 457-463.
- Adams, K. B., Matto, H. C., & Sanders, S. (2004). Confirmatory factor analysis of the geriatric depression scale. *The Gerontologist*, 44(6), 818-826.
- Alexopoulos, G. S., Abrams, R. C., Young, R. C., & Shamoian, C. A. (1988). Cornell scale for depression in dementia. *Biological psychiatry*, 23(3), 271-284.
- Algase, D. L., Beattie, E. R., Bogue, E. L., & Yao, L. (2001). The Algase Wandering Scale: initial psychometrics of a new caregiver reporting tool. *American Journal of Alzheimer's Disease & Other Dementias®*, 16(3), 141-152.
- Algase, D. L., Beattie, E. R., Song, J. A., Milke, D., Duffield, C., & Cowan, B. (2004). Validation of the Algase Wandering Scale (Version 2) in a cross cultural sample. *Aging and Mental Health*, 8(2), 133-142.
- Algase, D. L., Antonakos, C., Yao, L., Beattie, E. R., Hong, G. R. S., & Beel-Bates, C. A. (2008). Are wandering and physically nonaggressive agitation equivalent?. *The American Journal of Geriatric Psychiatry*, 16(4), 293-299.
- Alzheimer's Association. (2016). 2016 Alzheimer's disease facts and figures. *Alzheimer's & Dementia*, 12(4), 459-509.
- Åsberg, M., Montgomery, S. A., Perris, C., Schalling, D., & Sedvall, G. (1978). A comprehensive psychopathological rating scale. *Acta Psychiatrica Scandinavica*, 57(S271), 5-27.

- Auer, S. R., Monteiro, I. M., & Reisberg, B. (1996). The empirical behavioral pathology in Alzheimer's disease (E-BEHAVE-AD) rating scale. *International Psychogeriatrics*, 8(2), 247-266.
- Barca, M. L., Engedal, K., Selbaek, G., Knapskog, A. B., Laks, J., Coutinho, E., & Benth, J. Š. (2015). Confirmatory factor analysis of the Cornell scale for depression in dementia among patient with dementia of various degrees. *Journal of affective disorders*, 188, 173-178.
- Baumgarten, M., Becker, R., & Gauthier, S. (1990). Validity and reliability of the dementia behavior disturbance scale. *Journal of the American Geriatrics Society*, 38(3), 221-226.
- Beck, C., Heithoff, K., Baldwin, B., Cuffel, B., O'SULLIVAN, P., & Chumbler, N. (1997). Assessing disruptive behavior in older adults: The Disruptive Behavior Scale. *Aging & Mental Health*, 1(1), 71-80.
- Bentvelzen, A., Aerts, L., Seeher, K., Wesson, J., & Brodaty, H. (2017). A Comprehensive Review of the Quality and Feasibility of Dementia Assessment Measures: The Dementia Outcomes Measurement Suite. *Journal of the American Medical Directors Association*, 18(10), 826-837.
- Blazina, L., MA, L. T., & Rubin, E. (1995). The behavior rating scale for dementia of the Consortium to Establish a Registry for Alzheimer's Disease. *Am J psychiatry*, 152, 1349-1357.
- Bridges-Parlet, S., Knopman, D., & Thompson, T. (1994). A descriptive study of physically aggressive behavior in dementia by direct observation. *Journal of the American Geriatrics Society*, 42(2), 192-197.
- Burgio, L. D., Scilley, K., Hardin, J. M., Janosky, J., Bonino, P., Slater, S. C., & Engberg, R. (1994). Studying disruptive vocalization and contextual factors in the nursing home using computer-assisted real-time observation. *Journal of Gerontology*, 49(5), P230-P239.

- Callahan, C. M., Arling, G., Tu, W., Rosenman, M. B., Counsell, S. R., Stump, T. E., & Hendrie, H. C. (2012). Transitions in care for older adults with and without dementia. *Journal of the American Geriatrics Society*, 60(5), 813-820.
- Chan, D. C., Kasper, J. D., Black, B. S., & Rabins, P. V. (2003). Prevalence and correlates of behavioral and psychiatric symptoms in community-dwelling elders with dementia or mild cognitive impairment: the Memory and Medical Care Study. *International Journal of Geriatric Psychiatry*, 18(2), 174-182.
- Choi, S. S. W., Budhathoki, C., & Gitlin, L. N. (2017). Co-occurrence and predictors of three commonly occurring behavioral symptoms in dementia: agitation, aggression, and rejection of care. *The American Journal of Geriatric Psychiatry*, 25(5), 459-468.
- Cohen-Mansfield, J., Marx, M. S., & Rosenthal, A. S. (1989). A description of agitation in a nursing home. *Journal of gerontology*, 44(3), M77-M84.
- Cohen-Mansfield, J. (1991). Instruction manual for the Cohen-Mansfield agitation inventory (CMAI). *Research Institute of the Hebrew Home of Greater Washington*.
- Cohen-Mansfield, J., Marx, M. S., Dakheel-Ali, M., Regier, N. G., Thein, K., & Freedman, L. (2010). Can agitated behavior of nursing home residents with dementia be prevented with the use of standardized stimuli?. *Journal of the American Geriatrics Society*, 58(8), 1459-1464.
- Cummings, J. L., Mega, M., Gray, K., Rosenberg-Thompson, S., Carusi, D. A., & Gornbein, J. (1994). The Neuropsychiatric Inventory comprehensive assessment of psychopathology in dementia. *Neurology*, 44(12), 2308-2308.
- Cummings, J., Mintzer, J., Brodaty, H., Sano, M., Banerjee, S., Devanand, D. P., ... & Peskind, E. (2015). Agitation in cognitive disorders: International Psychogeriatric Association provisional consensus clinical and research definition. *International psychogeriatrics*, 27(1), 7-17.

- De Jonghe, J. F., Kat, M. G., Kalisvaart, C. J., & Boelaarts, L. (2003). Neuropsychiatric inventory questionnaire (NPI-Q): A validity study of the Dutch form. *Tijdschr Gerontol Geriatr*, 34(2), 74-77.
- Devanand, D. P., Brockington, C. D., Moody, B. J., Brown, R. P., Mayeux, R., Endicott, J., & Sackeim, H. A. (1992a). Behavioral syndromes in Alzheimer's disease. *International Psychogeriatrics*, 4(4), 161-184.
- Devanand, D. P., Miller, L., Richards, M., Marder, K., Bell, K., Mayeux, R., & Stern, Y. (1992b). The Columbia University scale for psychopathology in Alzheimer's disease. *Archives of Neurology*, 49(4), 371-376.
- De Medeiros, K., Robert, P., Gauthier, S., Stella, F., Politis, A., Leoutsakos, J., ... & Geda, Y. E. (2010). The Neuropsychiatric Inventory-Clinician rating scale (NPI-C): reliability and validity of a revised assessment of neuropsychiatric symptoms in dementia. *International Psychogeriatrics*, 22(6), 984-994.
- de Vugt, M. E., Stevens, F., Aalten, P., Lousberg, R., Jaspers, N., Winkens, I., ... & Verhey, F. R. (2004). Do caregiver management strategies influence patient behaviour in dementia?. *International journal of geriatric psychiatry*, 19(1), 85-92.
- Fernández, M., Gobartt, A. L., & Balaña, M. (2010). Behavioural symptoms in patients with Alzheimer's disease and their association with cognitive impairment. *BMC neurology*, 10(1), 87.
- Finkel, S. I., Lyons, J. S., & Anderson, R. L. (1993). A brief agitation rating scale (BARS) for nursing home elderly. *Journal of the American Geriatrics Society*, 41(1), 50-52.
- Fraser, J., Landreville, P., Voyer, P., & Carmichael, P. H. (2014). Factorial structure of the French version of the Nursing Home Behavior Problem Scale. *Canadian journal on aging= La revue canadienne du vieillissement*, 33(2), 163-175.

- Gates, D., Fitzwater, E., & Succop, P. (2003). Relationships of stressors, strain, and anger to caregiver assaults. *Issues in mental health nursing*, 24(8), 775-793.
- Gitlin, L. N., Marx, K. A., Stanley, I. H., Hansen, B. R., & Van Haitsma, K. S. (2014). Assessing neuropsychiatric symptoms in people with dementia: a systematic review of measures. *International psychogeriatrics*, 26(11), 1805-1848.
- Goekoop, J. G., Hoeksema, T., Klein, E. A. M., Klinkhamer, R. A., Gaalen, H. A. E., Londen, L., ... & Zwinderman, A. H. (1992). Multidimensional ordering of psychopathology. *Acta Psychiatrica Scandinavica*, 86(4), 306-312.
- Greene, J. G., Smith, R., Gardiner, M., & Timbury, G. C. (1982). Measuring behavioural disturbance of elderly demented patients in the community and its effects on relatives: a factor analytic study. *Age and Ageing*, 11(2), 121-126.
- Harwood, D. G., Ownby, R. L., Barker, W. W., & Duara, R. (1998). The factor structure of the Cornell Scale for Depression in Dementia among probable Alzheimer's disease patients. *The American Journal of Geriatric Psychiatry*, 6(3), 212-220.
- Hurley, A. C., Volicer, L., Camberg, L., Ashley, J., Woods, P., Odenheimer, G., ... & Mahoney, E. (1999). Measurement of observed agitation in patients with dementia of the Alzheimer type. *Journal of Mental Health and Aging*, 5(2), 117-134.
- Jeon, Y. H., Sansoni, J., Low, L. F., Chenoweth, L., Zapart, S., Sansoni, E., & Marosszeky, N. (2011). Recommended measures for the assessment of behavioral disturbances associated with dementia. *The American Journal of Geriatric Psychiatry*, 19(5), 403-415.
- Hamilton, M. (1960). A rating scale for depression. *Journal of neurology, neurosurgery, and psychiatry*, 23(1), 56.

- Helmes, E., Csapo, K. G., & Short, J. A. (1987). Standardization and validation of the multidimensional observation scale for elderly subjects (MOSES). *Journal of Gerontology*, 42(4), 395-405.
- Hurley, A. C., Volicer, L., Camberg, L., Ashley, J., Woods, P., Odenheimer, G., ... & Mahoney, E. (1999). Measurement of observed agitation in patients with dementia of the Alzheimer type. *Journal of Mental Health and Aging*, 5(2), 117-134.
- Ishii, S., Streim, J. E., & Saliba, D. (2012). A conceptual framework for rejection of care behaviors: review of literature and analysis of role of dementia severity. *Journal of the American Medical Directors Association*, 13(1), 11-23.
- Kaufer, D. I., Cummings, J. L., Ketchel, P., Smith, V., MacMillan, A., Shelley, T., ... & DeKosky, S. T. (2000). Validation of the NPI-Q, a brief clinical form of the Neuropsychiatric Inventory. *The Journal of neuropsychiatry and clinical neurosciences*, 12(2), 233-239.
- Kong, E. H. (2005). Agitation in dementia: concept clarification. *Journal of advanced nursing*, 52(5), 526-536.
- Kunik, M. E., Snow, A. L., Davila, J. A., Steele, A. B., Balasubramanyam, V., Doody, R. S., ... & Morgan, R. O. (2010). Causes of aggressive behavior in patients with dementia. *The Journal of clinical psychiatry*, 71(9), 1145-1152.
- Lam, C. L., Chan, W. C., Mok, C., Li, S. W., & Lam, L. C. (2006). Validation of the Chinese Challenging Behaviour Scale: clinical correlates of challenging behaviours in nursing home residents with dementia. *International journal of geriatric psychiatry*, 21(8), 792-799.
- Levin, H. S., High, W. M., Goethe, K. E., Sisson, R. A., Overall, J. E., Rhoades, H. M., ... & Gary, H. E. (1987). The neurobehavioural rating scale: assessment of the behavioural sequelae of head injury by the clinician. *Journal of Neurology, Neurosurgery & Psychiatry*, 50(2), 183-193.

- Linde, R. M., Stephan, B., Denning, T., & Brayne, C. (2014). Instruments to measure behavioural and psychological symptoms of dementia. *International journal of methods in psychiatric research*, 23(1), 69-98.
- Logsdon, R. G., Teri, L., Weiner, M. F., Gibbons, L. E., Raskind, M., Peskind, E., ... & Thai, L. J. (1999). Assessment of agitation in Alzheimer's disease: the agitated behavior in dementia scale. *Journal of the American Geriatrics Society*, 47(11), 1354-1358.
- Loreck, D. J., Bylsma, F. W., & Folstein, M. F. (1994). The Dementia Signs and Symptoms Scale: a new scale for comprehensive assessment of psychopathology in Alzheimer's disease. *The American Journal of Geriatric Psychiatry*, 2(1), 60-74.
- Lukoff, D., Liberman, R. P., & Nuechterlein, K. H. (1986). Symptom monitoring in the rehabilitation of schizophrenic patients. *Schizophrenia bulletin*, 12(4), 578-603.
- Moniz-Cook, E., Woods, R., Gardiner, E., Silver, M., & Agar, S. (2001). The Challenging Behaviour Scale (CBS): development of a scale for staff caring for older people in residential and nursing homes. *British Journal of Clinical Psychology*, 40(3), 309-322.
- Mahoney, E. K., Hurley, A. C., Volicer, L., Bell, M., Gianotis, P., Hartshorn, M., ... & Rheaume, Y. (1999). Development and testing of the Resistiveness to Care Scale. *Research in nursing & health*, 22(1), 27-38.
- Mungas, D., Weiler, P., Franzi, C., & Henry, R. (1989). Assessment of disruptive behavior associated with dementia: the Disruptive Behavior Rating Scales. *Topics in geriatrics*, 2(4), 196-202.
- Okura, T., Plassman, B. L., Steffens, D. C., Llewellyn, D. J., Potter, G. G., & Langa, K. M. (2011). Neuropsychiatric symptoms and the risk of institutionalization and death: the aging, demographics, and memory study. *Journal of the American Geriatrics Society*, 59(3), 473-481.

- Patel, V., & Hope, R. A. (1992). A rating scale for aggressive behaviour in the elderly—the RAGE. *Psychological medicine*, 22(1), 211-221.
- Palmstierna, T., & Wistedt, B. (1987). Staff observation aggression scale, SOAS: presentation and evaluation. *Acta Psychiatrica Scandinavica*, 76(6), 657-663.
- Perlman, C. M., & Hirdes, J. P. (2008). The aggressive behavior scale: a new scale to measure aggression based on the minimum data set. *Journal of the American Geriatrics Society*, 56(12), 2298-2303.
- Porsteinsson, A. P., Drye, L. T., Pollock, B. G., Devanand, D. P., Frangakis, C., Ismail, Z., ... & Pelton, G. (2014). Effect of citalopram on agitation in Alzheimer disease: the CitAD randomized clinical trial. *Jama*, 311(7), 682-691.
- Pruchno, R. A., Kleban, M. H., & Resch, N. L. (1988). Psychometric assessment of the multidimensional observation scale for elderly subjects (MOSES). *Journal of Gerontology*, 43(6), P164-P169.
- Rabins, P. V. (1984). Management of dementia in the family context. *Psychosomatics*, 25(5), 369-375.
- Ray, W. A., Taylor, J. A., Liechtenstein, M. J., & Meador, K. G. (1992). The nursing home behavior problem scale. *Journal of Gerontology*, 47(1), M9-M16.
- Regier, N. G., & Gitlin, L. N. (2017). Towards defining restlessness in individuals with dementia. *Aging & mental health*, 21(5), 543-552.
- Reisberg, B., Auer, S. R., & Monteiro, I. M. (1997). Behavioral pathology in Alzheimer's disease (BEHAVE-AD) rating scale. *International Psychogeriatrics*, 8(S3), 301-308.
- Rosen, W. G., Mohs, R. C., & Davis, K. L. (1984). A new rating scale for Alzheimer's disease. *The American journal of psychiatry*.

- Rosen, J., Burgio, L., Kollar, M., Cain, M., Allison, M., Fogleman, M., ... & Zubenko, G. S. (1994). The Pittsburgh Agitation Scale: a user-friendly instrument for rating agitation in dementia patients. *The American Journal of Geriatric Psychiatry*, 2(1), 52-59.
- Ruggeri, M., Koeter, M., Schene, A., Bonetto, C., Vázquez-Barquero, J. L., Becker, T., ... & EPSILON Study Group. (2005). Factor solution of the BPRS-expanded version in schizophrenic outpatients living in five European countries. *Schizophrenia research*, 75(1), 107-117.
- Ryden, M. B. (1988). Aggressive behavior in persons with dementia who live in the community. *Alzheimer Disease & Associated Disorders*, 2(4), 342-355.
- Schnaider Beerli, M., Werner, P., Davidson, M., & Noy, S. (2002). The cost of behavioral and psychological symptoms of dementia (BPSD) in community dwelling Alzheimer's disease patients. *International journal of geriatric psychiatry*, 17(5), 403-408.
- Shankar, K. K., Walker, M., Frost, D., & Orrell, M. W. (1999). The development of a valid and reliable scale for rating anxiety in dementia (RAID). *Aging & Mental Health*, 3(1), 39-49.
- Sinha, D., Zemlan, F. P., Nelson, S., Bienenfeld, D., Thienhaus, O., Ramaswamy, G., & Hamilton, S. (1992). A new scale for assessing behavioral agitation in dementia. *Psychiatry research*, 41(1), 73-88.
- Sommer, O. H., Kirkevold, Ø., Cvancarova, M., & Engedal, K. (2010). Factor analysis of the brief agitation rating scale in a large sample of Norwegian nursing home patients. *Dementia and geriatric cognitive disorders*, 29(1), 55-60.
- Spiegel, R., Brunner, C., Ermini-Fünfschilling, D., Monsch, A., Notter, M., Puxty, J., & Tremmel, L. (1991). A New Behavioral Assessment Scale for Geriatric Out-and In-Patients: the NOSGER (Nurses' Observation Scale for Geriatric Patients). *Journal of the American Geriatrics Society*, 39(4), 339-347.

- Steinberg, M., Shao, H., Zandi, P., Lyketsos, C. G., Welsh-Bohmer, K. A., Norton, M. C., ... & Tschanz, J. T. (2008). Point and 5-year period prevalence of neuropsychiatric symptoms in dementia: the Cache County Study. *International journal of geriatric psychiatry*, 23(2), 170-177.
- Teri, L., Truax, P., Logsdon, R., Uomoto, J., Zarit, S., & Vitaliano, P. P. (1992). Assessment of behavioral problems in dementia: the revised memory and behavior problems checklist. *Psychology and aging*, 7(4), 622.
- Torii, K., Nakaaki, S., Banno, K., Murata, Y., Sato, J., Tatsumi, H., ... & Furukawa, T. A. (2011). Reliability and validity of the Japanese version of the Agitated Behaviour in Dementia Scale in Alzheimer's disease: three dimensions of agitated behaviour in dementia. *Psychogeriatrics*, 11(4), 212-220.
- Tractenberg, R. E., Singer, C. M., Cummings, J. L., & Thal, L. J. (2003). The Sleep Disorders Inventory: an instrument for studies of sleep disturbance in persons with Alzheimer's disease. *Journal of sleep research*, 12(4), 331-337.
- Volicer, L., Bass, E. A., & Luther, S. L. (2007). Agitation and resistiveness to care are two separate behavioral syndromes of dementia. *Journal of the American Medical Directors Association*, 8(8), 527-532.
- Volicer, L., Van der Steen, J. T., & Frijters, D. H. (2009). Modifiable factors related to abusive behaviors in nursing home residents with dementia. *Journal of the American Medical Directors Association*, 10(9), 617-622.
- Volicer, L., Citrome, L., & Volavka, J. (2017). Measurement of agitation and aggression in adult and aged neuropsychiatric patients: review of definitions and frequently used measurement scales. *CNS spectrums*, 1-8.

- Wancata, J., Windhaber, J., Krautgartner, M., & Alexandrowicz, R. (2003). The consequences of non-cognitive symptoms of dementia in medical hospital departments. *The International Journal of Psychiatry in Medicine*, 33(3), 257-271.
- Wand, A. P. F., Peisah, C., Draper, B., & Brodaty, H. (2017). Understanding self-harm in older people: a systematic review of qualitative studies. *Aging & Mental Health*, 1-10.
- Yesavage, J. A., Brink, T. L., Rose, T. L., Lum, O., Huang, V., Adey, M., & Leirer, V. O. (1982). Development and validation of a geriatric depression screening scale: a preliminary report. *Journal of psychiatric research*, 17(1), 37-49.
- Yudofsky, S. C., Silver, J. M., Jackson, W., Endicott, J., & Williams, D. (1986). The Overt Aggression Scale for the objective rating of verbal and physical aggression. *The American journal of psychiatry*.
- Yudofsky, S. C., Kopecky, H. J., Kunik, M., Silver, J. M., & Endicott, J. (1997). The Overt Agitation Severity Scale for the objective rating of agitation. *The Journal of neuropsychiatry and clinical neurosciences*, 9(4), 541-548.

TABLES AND FIGURES

Figure 1. Search flowchart

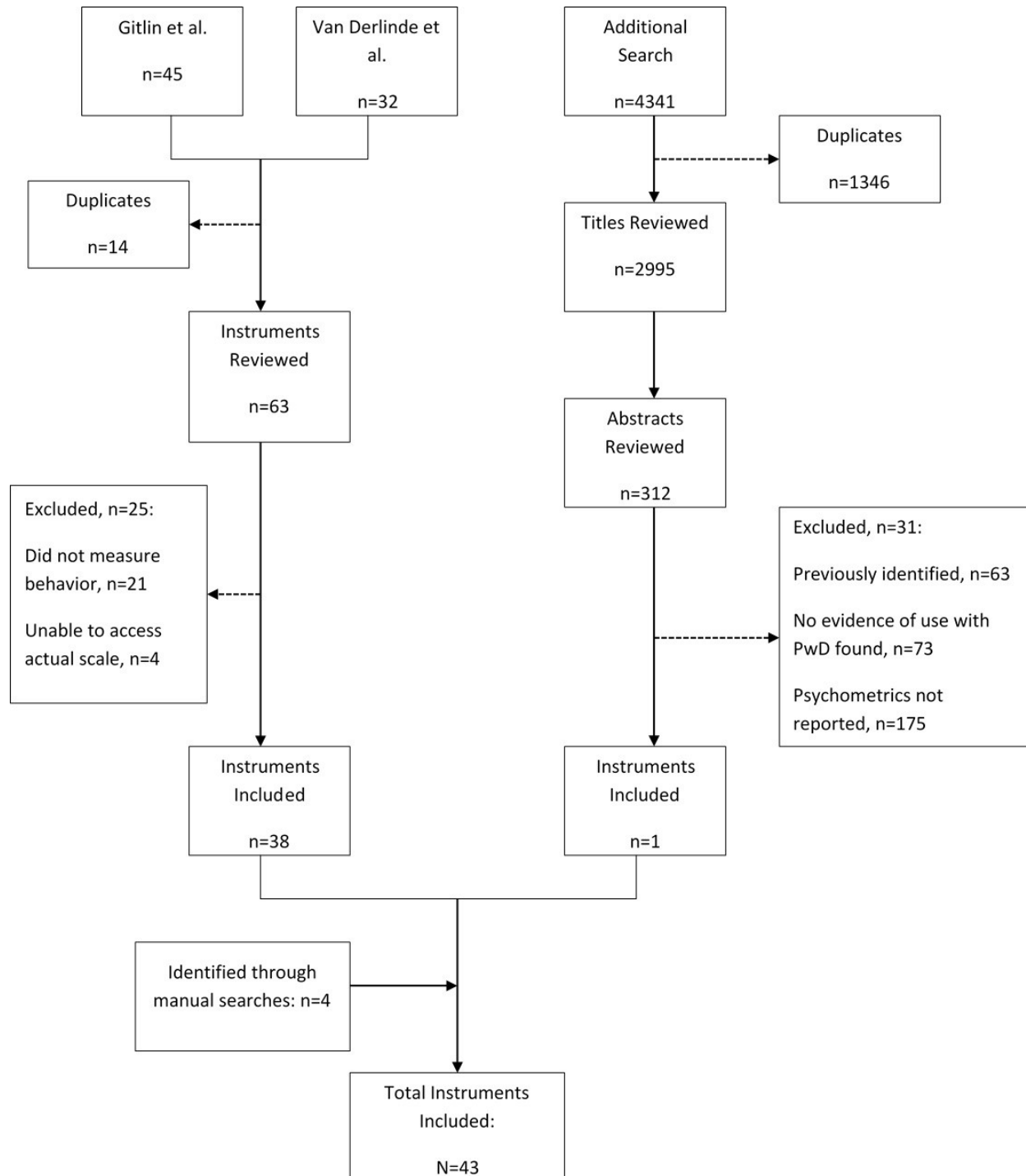


Table 1. Characteristics of BPSD Measures Included in the Review (n=43)

Scale (Author, Year)	Number of Items	Administration			Time Frame	Setting
		Who ^a	How ^b	To Whom ^c		
Composite Scales						
ADAS-Noncog: Alzheimer's Disease Assessment Scale (Rosen et al., 1984)	10	TI	I	D, P	1 week	SNF, Community
BEAM-D: Behavioral and Emotional Activities Manifested in Dementia (Sinha et al., 1992)	16	TI	I	D and P	Not specified	Community
BEHAVE-AD: Behavioral Pathology in Alzheimer's Disease (Reisberg et al., 1997)	26	TI	I	P	2 weeks	SNF, Outpatient setting
E-BEHAVE-AD: Empirical Behavioral Pathology in Alzheimer's Disease (Auer et al., 1996)	12	C	O	D	Current	Outpatient setting
BMDS: Behavior and Mood Disturbance Scale (Greene et al., 1982)	34	TI	I	P	Not specified	Community
BPRS-E: Expanded Brief Psychiatric Rating Scale (Lukoff et al., 1986)	24	C	I, O	D	Not specified	Inpatient, outpatient setting
BRSD: Behavioral Rating Scale for Dementia (Blazina et al., 1995)	46	TI	I	P	1 month	Various settings
BSSD: Behavioral Syndromes Scale for Dementia (Devanand et al., 1992a)	24	TI	I	P	1 week	Outpatient setting

CBS: Challenging Behavior Scale (Moniz-Cook et al., 2001)	25	N	O	D	8 weeks	SNF, Community
CPRS: Comprehensive Psychopathological Rating Scale (Åsberg et al., 1978)	65	TI	I	D	Varies (1 week, 1 day, or 1 month)	Not specified

Table 1. Continued

Scale (Author, Year)	Number of Items	Administration			Time Frame	Setting
		Who ^a	How ^b	To Whom ^c		
CUSPAD: Columbia University Scale for Psychopathology in Alzheimer's Disease (Devanand et al., 1992b)	27	TI	I	P	1 month	Outpatient setting
DBDS: Dementia Behavior Disturbance Scale (Baumgarten et al., 1990)	28	N, F	O	D	1 week	SNF, Community
DBS: Disruptive Behavior Scale (Beck et al., 1997)	45	N	O	D	Not specified	SNF
DBRS: Disruptive Behavior Rating Scale (Mungas et al., 1989)	21	N	O	D	1 week	SNF
DSS: Dementia Signs and Symptoms scale (Loreck et al., 1994)	43	TI	I	D, P	1 month	Inpatient, Outpatient setting
MOSES: Multi-dimensional Observation Scale for Elderly patients (Helmes et al., 1987)	40	N	O	D	1 week	Various settings
NHBPS: Nursing Home Behavior Problem Scale (Ray et al., 1992)	29	N	O	D	3 days	SNF

NOSGER: Nurses' Observation Scale for Geriatric Patients (Spiegel et al., 1991)	30	N, F	O	D	2 weeks	SNF, Community
NPI: Neuropsychiatric Inventory (Cummings et al., 1994)	81	TI	I	P	1 month	Not specified
NPI-C: Neuropsychiatric Inventory-Clinician (de Medeiros et al., 2010)	142	C	I	P, D, C	1 month	Not specified
NPI-Q: Neuropsychiatric Inventory-Questionnaire (Kaufer et al., 2000)	12	F	Q	P	1 month	Not specified
NRS: Neurobehavioral Rating Scale (Levin et al., 1987)	27	TI	I	D	Not specified	Not specified

Table 1. Continued

Scale (Author, Year)	Number of Items	Administration			Time Frame	Setting
		Who ^a	How ^b	To Whom ^c		
RMBPC: Revised Memory and Behavior Problem Checklist (Teri et al., 1992)	24	F	Q	P	1 week	Outpatient setting
<u>Specific Scales</u>						
<u>Aggression:</u>						
ABS: Aggressive Behavior Scale (Perlman & Hirdes, 2008)	4	N	O	D	7 days	SNF
OAS: Overt Aggression Scale (Yudofsky et al., 1986)	4	N, F	O	D	Current	Inpatient, SNF, Community
RAGE: Rating Scale for Aggressive Behavior in the Elderly (Patel & Hope, 1992)	21	N	O, CR	D	3 days	SNF

RAS: Ryden Aggression Scale (Ryden, 1988)	25	F	O	D	Past year	Community
SOAS: Staff Observation Aggression Scale (Palmstierna & Wistedt, 1987)	≥1	N	O	D	Current	SNF
<u>Agitation:</u>						
ABID: Agitated Behavior in Dementia scale (Logsdon et al., 1999)	16	F	O	D	2 weeks	Community
BARS: Brief Agitation Rating Scale (Finkel et al., 1993)	10	TI, N	I, O	N, D	2 weeks	SNF
CMAI -long form: Cohen-Mansfield Agitation Inventory (Cohen-Mansfield et al., 1989)	29	TI, N, NA, D	I, O	N, NA, D	1 week	SNF, Community
OASS: Overt Agitation Severity Scale (Yudofsky et al., 1997)	12	TO	O	D	Current	Inpatient setting

Table 1. Continued

Scale (Author, Year)	Number of Items	Administration			Time Frame	Setting
		Who ^a	How ^b	To Whom ^c		
PAS: Pittsburgh Agitation Scale (Rosen et al., 1994)	4	N	O	D	Current	Inpatient, SNF
SOAPD: Scale for Observation of Agitation in Persons with Dementia of the Alzheimer type (Hurley et al., 1999)	7	TO	O	D	Current	SNF
<u>Anxiety:</u>						
RAID: Rating Anxiety in Dementia (Shankar et al., 1999)	20	C	I, CR	N, P	2 weeks	Inpatient setting

Depression:

CSDD: Cornell Scale for Depression in Dementia (Alexopoulos et al., 1988)	19	C	I	D, P	1 week	Inpatient, SNF
GDS: Geriatric Depression Screening scale (Yesavage et al., 1983)	30	D, TI	Q, I	D	1 week	Inpatient, Community
HRS-D: Hamilton Rating Scale for Depression (Hamilton, 1960)	21	TI	I	D	Not specified	Not specified

Disruptive Vocalizations:

Computer-Assisted Real-Time Observation (Burgio et al., 1994)	1	TO	O	D	3 hours	SNF
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Rejection of Care:

RTC-DAT: Resistiveness to Care Scale (Mahoney et al., 1999)	13	N	O	D	Current	SNF
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Sleep Disorders:

SDI: Sleep Disorders Inventory (Tractenberg et al., 2003)	7	TI	I	P	2 weeks	Community
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Table 1. Continued

Scale (Author, Year)	Number of Items	Administration			Time Setting Frame
		Who ^a	How ^b	To Whom ^c	
<hr/>					
<u>Wandering:</u>					

AWS: Algase Wandering Scale (Algase et al., 2001)	23	TI, N, NA	I, O	N, NA, D	Not specified	SNF
AWS-V2: Algase Wandering Scale version 2 (Algase et al., 2004)	27	TI	I	N, NA	Not specified	SNF

^a N=nurse; NA=nursing assistant; F=family caregiver; TI=trained interviewer; TO=trained observer; C=clinician; D=person with dementia

^b I=interview; O=observation; Q=self-administered questionnaire; CR=chart review

^c D=person with dementia; P=proxy respondent; N=nurse; NA=nursing assistant; C=clinician

SNF= skilled nursing facility

Table 2. Summary of the Literature on Description of Rejection of Care, Aggression, and Agitation

Scale (Author, Year)	Agitation Items	Aggression Items	Rejection of Care Items	Factor Analysis Result
<u>General BPSD Scales</u>				
ADAS-Noncog (Rosen <i>et al.</i> , 1984)	<ul style="list-style-type: none"> • increased motor activity • tremors • pacing 	None	<ul style="list-style-type: none"> • uncooperativeness 	Factor analysis of ADAS-Noncog in persons with dementia with higher behavioral disturbances showed rejection of care item (uncooperativeness) and agitation item (hyperactivity, pacing) loaded on two different factors which were not specified. (Fernandez <i>et al.</i> , 2010)
BEAM-D (Sinha <i>et al.</i> , 1992)	<ul style="list-style-type: none"> • attention seeking behavior • wandering 	<ul style="list-style-type: none"> • hostility/aggression • destruction of property 	<ul style="list-style-type: none"> • noncompliance 	n/a
BEHAVE-AD (Reisberg <i>et al.</i> , 1997)	<p>In 'Activity disturbances' domain:</p> <ul style="list-style-type: none"> • wandering • purposeless activity 	<p>In 'Aggressiveness' domain:</p> <ul style="list-style-type: none"> • verbal outbursts • physical threats and/or violence 	<p>In 'Aggressiveness' domain:</p> <ul style="list-style-type: none"> • agitation (<i>"negativity including refusal to bathe, dress, continue walking, take medications"</i>) 	n/a

Table 2. (Continued)

Scale (Author, Year)	Agitation Items	Aggression Items	Rejection of Care Items	Factor Analysis Result
E-BEHAVE-AD (Auer <i>et al.</i> , 1996)	In 'Activity disturbance' domain: <ul style="list-style-type: none"> • pacing and wandering • repetitive activities 	In 'Aggressivity' domain: <ul style="list-style-type: none"> • verbal outbursts • physical threats and violence 	In 'Aggressivity' domain: <ul style="list-style-type: none"> • agitation (<i>"does not want to be helped, or other refusals indicative of negativity"</i>) 	Verbally and physically aggressive behaviors loaded on 'aggression' factor. Rejection of care item (agitation) loaded on 'agitation/anxiety' factor. 1 agitation item (pacing and wandering) loaded on 'activity disturbance' factor while another agitation item (repetitive activities) did not load on any of the factors in the analysis. (Harwood <i>et al.</i> , 1998)
BMDS (Greene <i>et al.</i> , 1982)	<ul style="list-style-type: none"> • wandering • appearing restless and agitated • pacing/wringing hands 	<ul style="list-style-type: none"> • becoming angry and threatening 	None	3 agitation items (wandering; appearing restless and agitated; pacing) loaded on 'active-disturbed' behavior factor; 1 aggression item loaded on 'mood-disturbance' factor (Greene <i>et al.</i> , 2010)
BPRS-E (Lukoff <i>et al.</i> , 1986)	<ul style="list-style-type: none"> • tension • motor hyperactivity 	<ul style="list-style-type: none"> • hostility 	None	1 aggression (hostility) and 1 agitation (motor hyperactivity) loaded on

'manic excitement' factor;
another agitation item
(tension) loaded on
anxiety/depression' factor.
(Ruggeri et al., 2005)

Table 2. (Continued)

Scale (Author, Year)	Agitation Items	Aggression Items	Rejection of Care Items	Factor Analysis Result
BRSD (Blazina <i>et al.</i> , 1995)	<ul style="list-style-type: none"> • agitation • restlessness • purposeless behavior • wandering • trying to leave home • repetitive behavior 	<ul style="list-style-type: none"> • verbal aggression • physical aggression 	<ul style="list-style-type: none"> • uncooperativeness 	Aggression items (verbal and physical aggressions) loaded on 'aggression' factor. 1 agitation item (agitation), 1 aggression item (verbal aggression), and 1 rejection of care item (uncooperativeness) all loaded on 'irritability/agitation' factor. (Blazina et al., 1995)
BSSD (Devanand <i>et al.</i> , 1992)	<p>In 'Disinhibition' domain:</p> <ul style="list-style-type: none"> • motor agitation • intrusiveness • wandering 	<p>In 'Disinhibition' domain:</p> <ul style="list-style-type: none"> • verbal aggression • physical aggression towards others 	<p>In 'Other clinical features' domain:</p> <ul style="list-style-type: none"> • stubbornness 	1 agitation item (motor agitation) loaded on 'sundowning' factor. 3 aggression items (verbal aggression, physical aggression toward others,

- physical aggression towards objects
- In 'Other clinical features' domain:
- repetitive movements
- In 'Sundowning' domain:
- increased agitation
- physical aggression toward objects) loaded on 'aggression' factor. Rejection of care item (stubbornness) loaded on 'aggression' factor as well. (Devanand et al., 1992)

Table 2. (Continued)

Scale (Author, Year)	Agitation Items	Aggression Items	Rejection of Care Items	Factor Analysis Result
CBS (Moniz-Cook et al., 2001)	<ul style="list-style-type: none"> • restlessness • wandering • noise making/ screaming • demands attention 	<ul style="list-style-type: none"> • physical aggression • verbal aggression • self-harm 	<ul style="list-style-type: none"> • non-compliance 	Physical aggression loaded on 'aberrant behaviors' factor. Verbal aggression loaded on 'verbally aggressive behaviors' factor. 'Self-harm' failed to load on any of the factors. 2 agitation items (restlessness and wandering) loaded on 'hyperactivity behaviors' factor and 1 agitation item (noise making/screaming) loaded on 'verbally aggressive behaviors' factor. Rejection of care item (non-compliance)

				loaded on 'hyperactivity' factor (Lam et al., 2006).
CPRS (Asberg et al., 1978)	<ul style="list-style-type: none"> • over activity • agitation 	<ul style="list-style-type: none"> • hostility 	None	1 agitation item (overactivity) loaded on 'motivational dysregulation' factor. Another agitation item (agitation) loaded on 'behavioral disintegration' factor. Aggression item (hostility) did not load on any of the 5 resulting factors (Goekoop et al., 1992).

Table 2. (Continued)

Scale (Author, Year)	Agitation Items	Aggression Items	Rejection of Care Items	Factor Analysis Result
CUSPAD: (Devanand et al., 1992)	<p>In 'Behavioral disturbances' domain:</p> <ul style="list-style-type: none"> • agitated or restless • wandering 	<p>In 'Behavioral disturbances' domain:</p> <ul style="list-style-type: none"> • verbal outbursts • physical threats and/or violence 	None	n/a
DBDS (Baumgarten et al., 1990)	<ul style="list-style-type: none"> • paces up and down • moves arms or legs in a restless or agitated way • wanders aimlessly • screams for no reason 	<ul style="list-style-type: none"> • verbally abusive or curses • makes physical attacks • destroys property or clothing • throws food 	<ul style="list-style-type: none"> • refuses to be helped with personal care • refuses to eat 	n/a

DBS (Beck et al., 1997)	<ul style="list-style-type: none"> • paces • makes repetitious noises • bangs objects non-destructively • excessive motor activity 	<ul style="list-style-type: none"> • uses hostile/accusatory language towards others • makes threats implying physical harm to self • injures self • makes threats implying harm to others • hits others • strikes another person with an object • uses a weapon • damages objects in the environment 	<ul style="list-style-type: none"> • refuses to eat/drink • spits medication 	n/a
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Table 2. (Continued)

Scale (Author, Year)	Agitation Items	Aggression Items	Rejection of Care Items	Factor Analysis Result
DBRS (Mungas et al., 1989)	<ul style="list-style-type: none"> • pacing • hand wringing • unable to sit/lie still • increased psychomotor activity • repeated expressions of distress • other signs of agitation • wandering 	<ul style="list-style-type: none"> • hitting • kicking • biting • using weapons • other physical aggression • yelling/screaming • swearing • threatening physical harm • other verbal aggression 	None	4 factors were identified: physical aggression, verbal aggression, wandering, and agitation. Items loading on each factor were not specified however (Mungas et al., 1989).

SS (Loreck et al., 1994)	<p>In 'Social disruptiveness' domain:</p> <ul style="list-style-type: none"> • disruptive/bothersome behaviors • wandering • shadowing <p>In 'Restlessness' domain:</p> <ul style="list-style-type: none"> • overactive behaviors • repetitive behaviors 	<p>In 'Aggressiveness' domain:</p> <ul style="list-style-type: none"> • verbal aggression • physical aggression 	<p>In 'Aggressiveness' domain:</p> <ul style="list-style-type: none"> • resistance to assistance 	n/a
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Table 2. (Continued)

Scale (Author, Year)	Agitation Items	Aggression Items	Rejection of Care Items	Factor Analysis Result
MOSES (Helmes et al., 1987)	None	<p>In 'Irritability' domain:</p> <ul style="list-style-type: none"> • verbal abuse of staff • verbal abuse of other residents • physical abuse of others 	<p>In 'Irritability' domain:</p> <ul style="list-style-type: none"> • cooperation with nursing care 	24 out of original 40 items were used for factor analysis; 2 aggression items (verbal abuse of staff and physical abuse of others) loaded on 'irritability' factor; Rejection of care item (co-operation with nursing care) was not included in this factor analysis. (Pruchno et al., 1988)

NHBPS (Ray et al., 1992)	In 'Irrational or restless behavior' domain:	In 'Dangerous behavior' domain:	In 'Uncooperative or aggressive behavior' domain:	5 unlabeled factors were revealed: 3 rejection of care items loaded together on Factor 1, along with 1 agitation item (screams, yells, or moans loudly) and 1 aggression item (argues, threatens, or curses). 2 agitation items (wanders; paces) loaded on Factor 3 and 2 agitation items (fidgets; does something over and over) loaded on Factor 5. Lastly, 1 aggression item (fights or is physically aggressive) loaded on Factor 4 (Fraser et al., 2014).
	<ul style="list-style-type: none"> • fidgets, is unable to sit still, restless • paces: walks or moves in wheelchair aimlessly back and forth • does something over and over, even though it doesn't make sense 	<ul style="list-style-type: none"> • tries to hurt self 	<ul style="list-style-type: none"> • resists care • uncooperative • refuses care 	
	In 'Annoying behavior' domain:	In 'Uncooperative or aggressive behavior' domain:		
	<ul style="list-style-type: none"> • asks for attention or help, even though it is not needed 	<ul style="list-style-type: none"> • fights or is physically aggressive • argues, threatens, or curses • screams, yells, or moans loudly 		
	In 'Inappropriate behavior' domain:	Not in any domain:		
	<ul style="list-style-type: none"> • wanders 	<ul style="list-style-type: none"> • damages or destroys things on purpose 		

Table 2. (Continued)

Scale (Author, Year)	Agitation Items	Aggression Items	Rejection of Care Items	Factor Analysis Result
NOSGER (Spiegel et al., 1991)	None	In 'Disturbing behavior' domain: <ul style="list-style-type: none"> • verbally or physically aggressive 	In 'Disturbing behavior' domain: <ul style="list-style-type: none"> • behaves stubbornly, does not follow instructions or rules 	n/a

NPI (Cummings et al., 1994)	In 'Aberrant motor behavior' domain: <ul style="list-style-type: none"> • pacing without purpose • repetitive activities • repetitive behaviors • excessive fidgeting 	In 'Agitation/Aggression' domain: <ul style="list-style-type: none"> • cursing or shouting angrily • slamming doors/kicking furniture/throwing things • attempting to hurt or hit others 	In 'Agitation/Aggression' domain: <ul style="list-style-type: none"> • resisting ADLs • stubbornness • uncooperative/resistive to help 	Agitation and aggression items loaded on 'hyperactivity' factor (Aalten et al., 2007).
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Scale (Author, Year)	Agitation Items	Aggression Items	Rejection of Care Items	Factor Analysis Result
NPI-C (de Medeiros et al., 2010)	In 'Agitation' domain: <ul style="list-style-type: none"> • being restless • fidgeting • pacing In 'Aberrant motor disturbance' domain: <ul style="list-style-type: none"> • pacing • repetitive dressing and undressing • repetitive activities • fidgeting • self-stimulating behaviors • moving with no purpose In 'Aberrant vocalization' domain: <ul style="list-style-type: none"> • making strange noises 	In 'Aggression' domain: <ul style="list-style-type: none"> • shouting or cursing • slamming door/kicking furniture/throwing things • attempting to hurt or hit others • grabbing/pushing/scratching others In 'Aberrant vocalizations' domain: <ul style="list-style-type: none"> • verbally abusive/threatening language • frequent verbal outbursts 	In 'Agitation' domain: <ul style="list-style-type: none"> • resisting ADLs • being stubborn • being uncooperative or resistive to help from others • refusing medications 	n/a

	<ul style="list-style-type: none"> • screaming without reason • talking excessively 			
NPI-Q (de Jonghe et al., 2003)	<p>In 'Motor disturbance' domain:</p> <ul style="list-style-type: none"> • repetitive activities, pacing 	None	<p>In 'Agitation/Aggression' domain:</p> <ul style="list-style-type: none"> • resistive to help from others 	n/a
NRS (Levin et al., 1987)	<ul style="list-style-type: none"> • agitation 	<ul style="list-style-type: none"> • hostility/uncooperativeness 	<ul style="list-style-type: none"> • hostility/uncooperativeness 	Agitation loaded on 'metacognition' factor and hostility/uncooperativeness loaded on 'somatic/anxiety' factor (Levin et al., 1987).
Scale (Author, Year)	Agitation Items	Aggression Items	Rejection of Care Items	Factor Analysis Result
RMBPC (Teri et al., 1992)	<ul style="list-style-type: none"> • talking loudly and rapidly 	<ul style="list-style-type: none"> • destroying property • aggressive to others verbally • threats to hurt oneself • threats to hurt others 	None	1 agitation item (talking loudly and rapidly) and 3 aggression items (destroying property; threats to hurt others; verbal aggression) on the 'disruption' factor. 1 aggression item (threats to hurt oneself) loaded on the 'depression' factor (Teri et al., 1992)

Symptom-Specific BPSD Scales

Aggressive Behavior:

ABS (Perlman et al., 2008)	None	<ul style="list-style-type: none"> • verbal abuse (e.g. screaming at others) • physical abuse (e.g. hitting others) 	<ul style="list-style-type: none"> • resisting care (e.g. pushing caregiver during ADL assistance) 	n/a
OAS (Yudofsky et al., 1986)	None	<ul style="list-style-type: none"> • verbal aggression • physical aggression against self • physical aggression against objects • physical aggression against other people 	None	n/a

Table 2. (Continued)

Scale (Author, Year)	Agitation Items	Aggression Items	Rejection of Care Items	Factor Analysis Result
RAGE (Patel & Hope, 1992)	None	<ul style="list-style-type: none"> • shouted/yelled/ screamed • swore/ used abusive language • threatened to harm others • pushed/shoved others 	<ul style="list-style-type: none"> • uncooperative or resisted help (e.g. whilst being given a bath or medication) 	3 factors: verbal aggression, physical aggression, anti-social behavior. Rejection of care item (uncooperative/resisted help) did not load strongly

		<ul style="list-style-type: none"> • destroyed property/ thrown things around • kicked others • hit others • bit/scratched others • used an object to hurt someone 		on any factor (Patel & Hope, 1992).
RAS (Ryden, 1988)	None	<p>In 'Physical aggression' domain:</p> <ul style="list-style-type: none"> • threatening gestures • pushing/ shoving • throwing an object • damaging property • pinching/ squeezing • hitting/ punching • elbowing • slapping • kicking • brandishing a weapon • striking a person with an object • spitting • scratching • biting • tackling • using a weapon <p>In 'Verbal aggression' domain:</p> <ul style="list-style-type: none"> • hostile, accusatory language • cursing directed at a person • verbal threats 	None	n/a

		<ul style="list-style-type: none"> • name calling 		
SOAS (Palmstierna et al., 1987)	None	<ul style="list-style-type: none"> • verbal aggression • physical aggression toward others • physical aggression toward objects 	<p><i>For each behavior, the observer is asked to report whether the behavior was provoked by ADL care or a medication administration attempt.</i></p>	n/a
<u>Agitated Behavior:</u>				
ABID (Logsdon et al., 1999)	<ul style="list-style-type: none"> • inappropriate screaming • restlessness/ fidgetiness/ inability to sit still • trying to leave home inappropriately • easily agitated or upset 	<ul style="list-style-type: none"> • verbally threatening or aggressive towards others • physically threatening or aggressive towards others • harmful to self • destroying property 	<ul style="list-style-type: none"> • refusing to accept appropriate help 	<p>3 items (physically aggressive toward others, harmful to self, destroying property) loaded on 'physically agitated behavior'. 1 aggression (verbally aggressive toward others) and 1 rejection of care (refusing to accept appropriate help) loaded on 'verbally agitated behavior' (Torii et al., 2011).</p>

Table 2. (Continued)

Scale (Author, Year)	Agitation Items	Aggression Items	Rejection of Care Items	Factor Analysis Result
BARS (Finkel et al., 1993)	<ul style="list-style-type: none"> • pacing/ aimless wandering • repetitious mannerisms • restlessness • making strange noises 	<ul style="list-style-type: none"> • hitting • grabbing • pushing • screaming 	None	<p>3 aggression items (hitting, pushing, grabbing) loaded on 'physically aggressive behavior' factor. 3 agitation items (wandering, restlessness, repetitive sentences) loaded on 'physically nonaggressive behavior' factor. 1 agitation item (making strange noises) loaded on 'verbal agitation' factor. Another agitation item (repetitive mannerisms) did not load on any of the factors, and 1 aggression item (screaming) was not included in the analysis (Sommer et al., 2010).</p>
CMAI-long form (Cohen-Mansfield et al., 1989)	<ul style="list-style-type: none"> • pacing and aimless wandering • constant unwarranted request for attention or help • making strange noises 	<ul style="list-style-type: none"> • cursing or verbal aggression • hitting • kicking 	<ul style="list-style-type: none"> • negativism (uncooperative, refusing) 	<p>4 factors were revealed in a community sample. 3 agitation items (pacing, repetitious mannerisms, general restlessness)</p>

- performing repetitious mannerisms
- general restlessness
- screaming (not directed toward others)
- grabbing onto people or things inappropriately
- pushing
- biting
- scratching
- hurting self or others
- tearing things or destroying property
- throwing things (not directed toward others)

loaded on 'physically non-aggressive behaviors' factor. 6 aggression items (hitting, pushing, scratching, grabbing, kicking, biting) loaded on 'physically aggressive behaviors' factor. 2 agitation items (making strange noises, screaming) and 1 aggression item (cursing) loaded on 'verbally aggressive behaviors' factor. 1 rejection of care item (negativism) loaded onto 'verbally non-aggressive behaviors' factor (Cohen-Mansfield, 1991).

OASS (Yudofsky et al., 1997)

In 'Vocalizations & oral/facial movements' domain:

- rocking, twisting, banging of head
- whimpering, whining, moaning, grunting

In 'Upper torso & upper extremity movements' domain:

In 'Vocalizations & oral/facial movements' domain:

- screaming, cursing, threatening

In 'Upper torso & upper extremity movements' domain:

- hitting at objects or others

In 'Lower extremity movements' domain:

None

n/a

- tapping fingers, fidgeting, or wringing of hands
- rocking back and forth, bobbing up and down, twisting of torso
- kicking at objects or others

In 'Lower extremity movements' domain:

- tapping toes or heel, clenching toes
- shaking legs, tapping knees and/or thighs
- pacing, wandering

PAS (Rosen et al., 1994)

- aberrant vocalization (repetitive requests or complaints, moaning, screaming)
- motor agitation (pacing, wandering, picking at objects)
- aggressiveness (verbal threats, threatening gestures, physical toward property, physical toward self)
- resisting care (verbal/gesture of refusal, pushing away, striking out at caregiver)

n/a

SOAPD (Hurley et al., 1999)

- total body movements (restlessness, pacing, repetitively walking back and forth)
- up/down movements (getting up repetitively, sitting up repetitively)
- repetitive body motions in place

None

None

2 factors: physical component and verbal component. 1 agitation item (high-pitched or loud noise) and 1 aggression item (negative words) loaded on the 'verbal' factor. 3 agitation items

- (rocking, tapping fingers/feet)
- high-pitched or loud noise (calling out, shouting/yelling, crying out, screaming)
- outward motions (repetitive behaviors involving contact with an object or a person)

(total body movements, up/down movements, repetitive body motions in place) and 1 aggression item (outward motions) loaded on the 'physical' factor (Hurley et al., 1999).

Anxiety:

RAID (Shankar et al., 1999)

In 'Motor tension' domain:

- restlessness (fidgeting, cannot sit still, pacing, wringing hands, picking clothes)

None

None

1 agitation item (restlessness) loaded on Factor 2 (unlabeled) along with 'irritability' and 'palpitations' (Shankar et al., 1999).

Table 2. (Continued)

Scale (Author, Year)	Agitation Items	Aggression Items	Rejection of Care Items	Factor Analysis Result
<u>Depression:</u>				
CSDD (Alexopoulos et al., 1988)	In 'Behavioral disturbance' domain: • agitation (restlessness, handwringing, hairpulling)	None	None	Agitation loaded on 'general depression' factor (Harwood, 1998), 'psychosis' factor (Ownby, 2001), and 'retardation' factor (Barca et al., 2015).
GDS (Yesavage et al., 1983)	• restless and fidgety	None	None	1 agitation item (restlessness) loaded on 'agitation' factor (Adams et al., 2004). Note: 'Restlessness' item is not included in the short form of GDS.
HRS-D (Hamilton, 1960)	• agitation (restlessness associated with anxiety)	None	None	Agitation loaded on Factor 2 (unlabeled) along with initial and delayed insomnia, hypochondriasis, weight loss, and gastro-intestinal

symptoms (Hamilton, 1960).

Disruptive Vocalizations:

CABOS (Burgio et al., 1994)

- *moaning*
- *repeated requests for attention*
- *repetitious words or sentences*
- *screaming*
- *cursing*

None

Note: They defined disruptive vocalization as "screaming, cursing, complaining, negativism, moaning, paranoid verbalization, repeated requests for attention, repetitious words or sentences, singing outside of an organized activity, and self-talk regardless of volume". They didn't differentiate among the different types of DV.

Rejection of Care:

RTC-DAT (Mahoney et al., 1999) None

None. *Aggressive behaviors occurring within the context of personal care are categorized as resistive behaviors (rejection of care) in this scale.*

- hold back
- grab object
- say no
- adduct
- grab person
- pull away
- clench
- cry
- scream
- turn away
- push away
- hit/kick
- threaten

3 factors: warding off/taking on, vocal/emotional resistance, protective/reflexive resistance (Mahoney et al., 1999).

Sleep Disorders:

SDI (Tractenberg et al., 2003)

- night-time wandering/pacing

None

None

n/a

Wandering:

AWS (Algase et al., 2001)

- increased spontaneous walking
- paces up and down
- walks around restlessly
- walks about aimlessly

None

- walks away from table at meals

3 agitation items (increased spontaneous walking; paces up and down; walks around restlessly) loaded on 'persistent walking' factor; 1 agitation item (walks about aimlessly) and 1 rejection of care item (walks away from table during meals) loaded on

				'spatial disorientation' factor (Algase et al., 2001).
AWS-V2 (Algase et al., 2004)	<ul style="list-style-type: none"> • increased spontaneous walking • paces up and down • walks around restlessly • walks about aimlessly 	None	<ul style="list-style-type: none"> • tries to leave table during meals 	3 agitation items (paces up and down, increased spontaneous walking, walks around restlessly) loaded on 'persistent walking' factor. 1 agitation item (walks about aimlessly) loaded on 'spatial disorientation' factor. Rejection of care (tries to leave the table during meals) did not load on any factor (Algase et al., 2004).

ABID = Agitated Behaviour in Dementia; ABS = Aggressive Behavior Scale; ADAS-Noncog = Alzheimer's Disease Assessment Scale Non-Cognitive Subscale; AWS = Algase Wandering Scale; AWS-V2 = Algase Wandering Scale Version 2; BARS = Brief Agitation Rating Scale; BEAM-D = Behavioral and Emotional Activities Manifested in Dementia; BEHAVE-AD = Behavioral Pathology in Alzheimer's Disease Scale; E-BEHAVE-AD = Empirical Behavioral Pathology in Alzheimer's Disease Scale; BMDS = Behavioral and Mood Disturbance Scale; BPSD = Behavioral and Psychological Symptoms of Dementia; BPRS-E = Brief Psychiatric Rating System-Expanded Version; BRSD = Behavioral Rating Scale for Dementia; BSSD = Behavioral Syndromes Scale for Dementia; CBS = Challenging Behavior Scale; CMAI = Cohen-Mansfield Agitation Inventory; CPRS = Comprehensive Psychopathological Rating Scale; CSDD = Cornell Scale for Depression in Dementia; CUSPAD = Columbia University Scale for Psychopathology in Alzheimer's Disease; DBDS = Dementia Behavior Disturbance Scale; DBS = Disruptive Behavior Scale; DBRS = Disruptive Behavior Rating Scale; DSS = Dementia Signs and Symptoms Scale; GDS = Geriatric Depression Scale; HRS-D = Hamilton Rating Scale for Depression; MOSES = Multidimensional Observation Scale for Elderly Subjects; NHBPS = Nursing Home Behavior Problem Scale; NOSGER = Nurses' Observation Scale for Geriatric Patients; NPI = Neuropsychiatric Inventory; NPI-C = Neuropsychiatric Inventory Clinician; NPI-Q = Neuropsychiatric

Inventory Questionnaire; NRS = Neurobehavioural Rating Scale; OAS = Overt Aggression Scale; OASS = Overt Agitation Severity Scale; PAS = Pittsburgh Agitation Scale; RAGE = Rating Scale for Aggressive Behavior in the Elderly; RAID = Rating Anxiety in Dementia; RAS = Ryden Aggression Scale; RMBPC = Revised Memory and Behavior Problems Checklist; RTC-DAT = Resistiveness to Care-Dementia of the Alzheimer Type; SDI = Sleep Disorders Inventory; SOAPD = Scale to Assess Observed Agitation in Persons with Dementia of the Alzheimer Type; SOAS = Staff Observation Aggression Scale

Table 3. Overview of items related to rejection of care, aggression, and agitation that are measured by the instruments

	Rejection of Care								
	Un-cooperative-ness	Resistance to care/ Resistiveness to care/ Resisting care	Care refusal /Refusing to accept help	Stubborn-ness	Non-compliance	Agitation	Negativity/ Negativism	Refusing medications/ Spitting medications	Refusing to eat/ Leaving table during meals
General measures									
ADAS-Noncog	•								
BEAM-D					•				
BEHAVE-AD						•	•		
E-BEHAVE-AD						•	•		
BMDS									
BPRS-E									
BRSD	•								
BSSD				•					
CBS					•				
CPRS									

[illegible]

(Continues)

Table 3. (Continued)

Rejection of Care									
	Un-cooperative-ness	Resistance to care/	Care refusal	Stubborn-ness	Non-compliance	Agitation	Negativity/Negativism	Refusing medications/	Refusing to eat/
		Resistiveness to care/	/Refusing to accept help					Spitting medications	Leaving table during meals
		Resisting care							
Symptom-specific measures									
Aggression									
ABS		●							
OAS									
RAGE	●	●							
RAS									
SOAS ^a									
Agitation									
ABID			●						

BARS

CMAI

OASS

PAS

SOAPD

Anxiety

RAID

Depression

CSDD

GDS

HRS-D

**Disruptive
vocalization**

CABOS

**Rejection
of care**

RTC-DAT^b

(Continues)

Table 3. (Continued)

	Rejection of Care								
	Un-cooperative-ness	Resistance to care/ Resistiveness to care/ Resisting care	Care refusal /Refusing to accept help	Stubborn-ness	Non-compliance	Agitation	Negativity/ Negativism	Refusing medications/ Spitting medications	Refusing to eat/ Leaving table during meals
<i>Sleep disorders</i>									
SDI									
<i>Wandering</i>									
AWS									●
AWS-V2									●

Notes:

^a For each behavior, the observer is asked to report whether the behavior was provoked by ADL care or a medication administration attempt, in which case aggressive behaviors should be rejection of care.

^b This rejection of care scale includes 13 (mostly aggressive) behaviors ranging from 'saying no' to 'grabbing person', 'screaming/yelling' and 'clenching mouth'. However, since these behaviors occur within the context of personal care, they are rejection of care.

	Aggression					
	Verbal aggression	Physical aggression	Destruction of property/ Aggression toward objects	Threatening behaviors	Hostility	Self-harm
General measures						
ADAS-Noncog						
BEAM-D			•		•	
BEHAVE-AD	•	•		•		
E-BEHAVE-AD	•	•		•		
BMDS				•		
BPRS-E					•	
BRSD	•	•				

(Continues)

Table 3. (Continued)

	Aggression					
	Verbal aggression	Physical aggression	Destruction of property/ Aggression toward objects	Threatening behaviors	Hostility	Self-harm
BSSD	•	•	•			
CBS	•	•				•
CPRS					•	
CUSPAD	•	•		•		
DBDS	•	•	•			
DBS	•	•	•	•		•
DBRS	•	•		•		
DSS	•	•				
MOSES	•	•				
NHBPS	•	•	•	•		•
NOSGER	•	•				

NPI			
NPI-C			
NPI-Q			
NRS			
RMBPC			
Symptom-specific measures			
Aggression			
ABS			
OAS			
RAGE			
RAS			
SOAS			
Agitation			
ABID			
BARS			
CMAI			

Table 3. (Continued)

	Aggression					
	Verbal aggression	Physical aggression	Destruction of property/ Aggression toward objects	Threatening behaviors	Hostility	Self-harm
OASS	•	•	•			
PAS	•		•			•
SOAPD						
Anxiety						
RAID						
Depression						
CSDD						
GDS						
HRS-D						
Disruptive vocalization						

CABOS



Rejection

of care

RTC-DAT

***Sleep
disorders***

SDI

Wandering

AWS

AWS-V2

(Continues)

Table 3. (Continued)

	Agitation								
	Pacing/ Purposeless behaviors	Wandering/ Trying to leave home inappropriately	Repetitive activities/ Repetitious mannerism	Talking excessively, loudly, or rapidly	Increased motor activity/ Motor hyperactivity	Restlessness /Inability to sit still/ Fidgetiness	Agitation	Noise making/ Screaming (not directed toward others)	Attention seeking behavior
General measures									
ADAS-Noncog	•				•				
BEAM-D		•							•
BEHAVE-AD	•	•							
E-BEHAVE-AD	•	•	•						
BMDS	•	•				•	•		
BPRS-E					•				
BRSD	•	•	•			•	•		
BSSD		•	•				•		•
CBS		•				•		•	•
CPRS					•		•		

CUSPAD		•				•	•	
DBDS	•	•				•	•	•
DBS	•				•			•
DBRS	•	•			•	•	•	
DSS		•	•		•			•
MOSES								
NHBPS	•	•	•			•		•
NOSGER								
NPI	•		•			•		
NPI-C	•		•	•		•		•
NPI-Q	•		•					
NRS							•	
RMBPC				•				
Symptom-specific measures								
Aggression								
ABS								

(Continues)

Table 3. (Continued)

	Agitation								
	Pacing/ Purposeless behaviors	Wandering/ Trying to leave home inappropriately	Repetitive activities/ Repetitious mannerism	Talking excessively, loudly, or rapidly	Increased motor activity/ Motor hyperactivity	Restlessness /Inability to sit still/ Fidgetiness	Agitation	Noise making/ Screaming (not directed toward others)	Attention seeking behavior
OAS									
RAGE									
RAS									
SOAS									
Agitation									
ABID		•				•	•	•	
BARS	•	•	•			•		•	
CMAI	•	•	•			•		•	•
OASS	•	•				•		•	
PAS	•	•					•	•	
SOAPD	•		•			•		•	

Anxiety

RAID



Depression

CSDD



GDS



HRS-D



***Disruptive
vocalization***

CABOS



***Rejection
of care***

RTC-DAT

***Sleep
disorders***

SDI



Wandering

AWS



AWS-V2



ABID = Agitated Behaviour in Dementia; ABS = Aggressive Behavior Scale; ADAS-Noncog = Alzheimer's Disease Assessment Scale Non-Cognitive Subscale; AWS = Algate Wandering Scale; AWS-V2 = Algate Wandering Scale Version 2; BARS = Brief Agitation Rating Scale; BEAM-D = Behavioral and Emotional Activities Manifested in Dementia; BEHAVE-AD = Behavioral Pathology in Alzheimer's Disease Scale; E-BEHAVE-AD = Empirical Behavioral Pathology in Alzheimer's Disease Scale; BMDS = Behavioral and Mood Disturbance Scale; BPSD = Behavioral and Psychological Symptoms of Dementia; BPRS-E = Brief Psychiatric Rating System-Expanded Version; BRSD = Behavioral Rating Scale for Dementia; BSSD = Behavioral Syndromes Scale for Dementia; CABOS = Computer-assisted Behavioral Observation Systems; CBS = Challenging Behavior Scale; CMAI = Cohen-Mansfield Agitation Inventory; CPRS = Comprehensive Psychopathological Rating Scale; CSDD = Cornell Scale for Depression in Dementia; CUSPAD = Columbia University Scale for Psychopathology in Alzheimer's Disease; DBDS = Dementia Behavior Disturbance Scale; DBS = Disruptive Behavior Scale; DBRS = Disruptive Behavior Rating Scale; DSS = Dementia Signs and Symptoms Scale; GDS = Geriatric Depression Scale; HRS-D = Hamilton Rating Scale for Depression; MOSES = Multidimensional Observation Scale for Elderly Subjects; NHBPS = Nursing Home Behavior Problem Scale; NOSGER = Nurses' Observation Scale for Geriatric Patients; NPI = Neuropsychiatric Inventory; NPI-C = Neuropsychiatric Inventory Clinician; NPI-Q = Neuropsychiatric Inventory Questionnaire; NRS = Neurobehavioural Rating Scale; OAS = Overt Aggression Scale; OASS = Overt Agitation Severity Scale; PAS = Pittsburgh Agitation Scale; RAGE = Rating Scale for Aggressive Behavior in the Elderly; RAID = Rating Anxiety in Dementia; RAS = Ryden Aggression Scale; RMBPC = Revised Memory and Behavior Problems Checklist; RTC-DAT = Resistiveness to Care-Dementia of the Alzheimer Type; SDI = Sleep Disorders Inventory; SOAPD = Scale to Assess Observed Agitation in Persons with Dementia of the Alzheimer Type; SOAS = Staff Observation Aggression Scale

Table 4. Overview of instruments with items related to rejection of care, aggression, and agitation									
	General BPSD scales (N=23)	Aggression scales (N=5)	Agitation scales (N=6)	Anxiety scale (N=1)	Depression scales (N=3)	Disruptive vocalization scale (N=1)	Rejection of care scale (N=1)	Sleep disorders scale (N=1)	Wandering scales (N=2)
Instruments that include separate items related to rejection of care, aggression, and agitation*	BEAM-D; BEHAVE-AD; E- BEHAVE-AD; BRSD; BSSD; CBS; DBDS; DBS; DSS; NHBPS; NPI; NPI-C; NRS		ABID; CMAI; PAS						
Instruments that do <u>not</u> include items related to rejection of care	BMDS; BPRS-E; CPRS; CUSPAD; DBRS; RMBPC		BARS; OASS			CABOS			
Instruments that do <u>not</u> include items related to aggression	ADAS-Noncog; NPI-Q								AWS; AWS- V2
Instruments that do <u>not</u> include items related to agitation	MOSES; NOSGER	ABS; RAGE; SOAS							

Instruments that only include items related to rejection of care							RTC-DAT		
Instruments that only include items related to aggression		OAS; RAS							
Instruments that only include items related to agitation			SOAPD	RAID	CSDD; GDS; HRS-D				

* These scales include items related to all three behaviors but their categorization of these items may not correspond to our categorization scheme.

ABID = Agitated Behaviour in Dementia; ABS = Aggressive Behavior Scale; ADAS-Noncog = Alzheimer's Disease Assessment Scale Non-Cognitive Subscale; AWS = Algase Wandering Scale; AWS-V2 = Algase Wandering Scale Version 2; BARS = Brief Agitation Rating Scale; BEAM-D = Behavioral and Emotional Activities Manifested in Dementia; BEHAVE-AD = Behavioral Pathology in Alzheimer's Disease Scale; E-BEHAVE-AD = Empirical Behavioral Pathology in Alzheimer's Disease Scale; BMDS = Behavioral and Mood Disturbance Scale; BPSD = Behavioral and Psychological Symptoms of Dementia; BPRS-E = Brief Psychiatric Rating System-Expanded Version; BRSD = Behavioral Rating Scale for Dementia; BSSD = Behavioral Syndromes Scale for Dementia; CABOS = Computer-assisted Behavioral Observation Systems; CBS = Challenging Behavior Scale; CMAI = Cohen-Mansfield Agitation Inventory; CPRS = Comprehensive Psychopathological Rating Scale; CSDD = Cornell Scale for Depression in Dementia; CUSPAD = Columbia University Scale for Psychopathology in Alzheimer's Disease; DBDS = Dementia Behavior Disturbance Scale; DBS = Disruptive Behavior Scale; DBRS = Disruptive Behavior Rating Scale; DSS = Dementia Signs and Symptoms Scale; GDS = Geriatric Depression Scale; HRS-D = Hamilton Rating Scale for Depression; MOSES = Multidimensional Observation Scale for Elderly Subjects; NHBPS = Nursing Home Behavior Problem Scale; NOSGER = Nurses' Observation Scale for Geriatric Patients; NPI = Neuropsychiatric Inventory; NPI-C = Neuropsychiatric

Inventory Clinician; NPI-Q = Neuropsychiatric Inventory Questionnaire; NRS = Neurobehavioural Rating Scale; OAS = Overt Aggression Scale; OASS = Overt Agitation Severity Scale; PAS = Pittsburgh Agitation Scale; RAGE = Rating Scale for Aggressive Behavior in the Elderly; RAID = Rating Anxiety in Dementia; RAS = Ryden Aggression Scale; RMBPC = Revised Memory and Behavior Problems Checklist; RTC-DAT = Resistiveness to Care-Dementia of the Alzheimer Type; SDI = Sleep Disorders Inventory; SOAPD = Scale to Assess Observed Agitation in Persons with Dementia of the Alzheimer Type; SOAS = Staff Observation Aggression Scale

CHAPTER 3: MANUSCRIPT 2

Co-occurrence and predictors of three commonly occurring behavioral symptoms in dementia: Agitation, aggression, and rejection of care

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ABSTRACT

Objective: To investigate co-occurrences of agitation, aggression, and rejection of care in community-dwelling families living with dementia. **Methods:** Cross-sectional, secondary analysis from a randomized controlled trial testing a non-pharmacological intervention to reduce behavioral symptoms. We examined frequency of occurrence of presenting behaviors at baseline and their combination. Omnibus tests compared those exhibiting combinations of behaviors on contributory factors. Multinomial logistic regression analyses examined relationships of contributory factors to combinations of behaviors. **Results:** Of 272 persons with dementia (PwDs), 41 (15%) had agitation alone (Agi), 3 (1%) had aggression alone, 5 (2%) had rejection of care alone. For behavioral combinations, 65 (24%) had agitation and aggression (Agi+Aggr), 35 (13%) had agitation and rejection (Agi+Rej), 1 (0%) had aggression and rejection, and 106 (39%) had all three behaviors (All). Four behavioral subgroups (Agi, Agi+Aggr, Agi+Rej, and All) were examined. Kruskal-Wallis test showed that there were significant group differences in PwD cognition, functional dependence, and caregiver frustration. PwDs in Agi+Rej and All were more cognitively impaired than those in Agi and Agi+Aggr. Also, caregivers in All were more frustrated than those in Agi. In logistic regression analyses, compared to Agi, greater cognitive impairment was a significant predictor of Agi+Rej and All, but not Agi+Aggr. In contrast, greater caregiver frustration was a significant predictor of Agi+Aggr and All, but not Agi+Rej. **Conclusion:** We found agitation, aggression, and rejection are common but distinct behaviors. Combinations of these behaviors have different relationships with contributory factors, suggesting the need for targeting treatment approaches to clusters.

Behavioral symptoms are commonly observed in persons with dementia (PwDs) with most exhibiting one or more behavioral symptoms at some point over the course of the disease.¹ Behavioral symptoms have negative consequences for both PwDs and caregivers. For PwDs, their occurrences and severity are associated with decreased independence in activities of daily living and quality of life, and if untreated, more rapid disease progression, and risk for nursing home placement.^{2,3} For caregivers, contending with behavioral symptoms is associated with increased caregiver burden and care costs.^{3,4} Although behavioral symptoms are considered a hallmark of the disease process, much is unknown about their co-occurrences and correlates.

The purpose of this study is to examine the inter-relationships of three commonly occurring behaviors, agitation, aggression and rejection of care in a sample of community-dwelling families living with dementia.

Each of these behaviors has either been variably defined, not distinguished from the other, or subsumed as a form of “agitation”. Agitation typically refers to “inappropriate verbal, vocal, or motor activity that is not explained by needs or confusion per se.”⁵ It is a broad rubric which can include a wide range of behavioral symptoms including aggression and rejection of care.

Aggression has been referred to as “an overt act, involving the delivery of noxious stimuli to (but not necessarily aimed at) another object, organism or self, which is clearly not accidental”.⁶ The distinction between agitation and aggression has not always been clear in research and/or measurement tools.⁷ Widely used rating scales such as the Cohen-Mansfield Agitation Inventory (CMAI)⁸ and the Neuropsychiatric Inventory (NPI)⁹ subsume aggressive type behaviors as a form of agitation although recent research suggests that agitated type

behaviors (e.g., wandering, restlessness, and hyperactivity).may be conceptually distinct from and occur without aggression.^{7,10,11}

Rejection of care has been referred to as “the repertoire of behaviors with which persons with dementia withstand or oppose the efforts of a caregiver”.¹² This behavior has been described variably as noncompliance, uncooperative behavior, and resistiveness to care.¹³ Rejection of care is distinct from aggression in that the underlying intent of PwD is to reject or refuse needed care but not to harm others although aggressiveness may be manifested in rejecting care.^{4,13} Rejection of care has also been considered a form of agitation. The NPI⁹ uses this behavior as a screening item for the domain of agitation/aggression. More recently, there has been an attempt to differentiate rejection of care from agitation with some suggesting that these may be two separate behavioral syndromes that occur differentially with disease severity (Volicer, 2007). Also argued is that the term agitation should be reserved for behaviors occurring in situations that do not involve interactions with caregivers.^{7,14}

Agitation, aggression, and rejection of care are among the behavioral symptoms that are most prevalent and troublesome to caregivers. Agitation has been associated with caregiver burden, decreased quality of life for PwDs as well as caregivers, restraint use, and institutionalization.¹⁵ The prevalence of agitation in community-dwelling PwDs varies widely across studies, ranging from 45%¹⁶ to 90%.¹⁷

Aggression is often associated with severe caregiver stress, aggressive caregiver reaction, psychotropic drug use, and risk for institutionalization.⁴ A community-based study determined a prevalence of aggression to be 41%.⁴ Rejection of care has also been reported as frequently occurring among nursing home residents with dementia (71%),¹⁸ the most distressful behavioral

symptom for family caregivers,¹⁹ and the behavior nursing home staff find the most difficult to cope with.²⁰

Despite the importance and high prevalence of these behaviors, the extent to which they are distinct, overlap and/or co-occur is unclear. Distinguishing among these three behavioral symptoms is important in that they may have different etiologies and require distinct treatment strategies. Limitations of previous research concerning these behaviors include lack of involving community-dwelling PwDs, not distinguishing rejection and/or aggression from agitation, and including only a small number of potential risk factors.^{21,22} To our knowledge, this is one of the first studies to examine the co-occurrences of these three behaviors and identify factors associated with different combinations of co-occurrence among community-dwelling PwDs.

To identify predictors of behavioral occurrences, we used a conceptual model linking neurodegeneration to behavioral symptoms.³ According to this model, interactions between neurodegeneration, and factors associated with PwD, caregiver, and the environment, may increase vulnerability to stressors leading to behavioral symptoms. Thus, we examined cognitive status, functional status, and pain of PwDs, and caregiver burden and frustration as potential predictors of co-occurring behavioral symptoms. As the data set utilized did not include measures of environmental factors, we were unable to examine this domain. This study posed three descriptive questions: what is the frequency of occurrence of each behavior and their combination; are there differentiating characteristics for each group of co-occurring behaviors; and what factors are associated with which combinations of behaviors?

METHODS

Participants

Data for this study were derived from Project ACT, a randomized controlled trial testing the effectiveness of a home-based intervention to minimize behaviors of PwDs.¹⁹ The research methods and study outcomes have been described in detail elsewhere.²³ In brief, the study sample consisted of 272 community-dwelling PwDs and their caregivers. Participants were recruited between December 2003 and March 2007. Caregivers living with PwDs and reporting one or more behavioral symptoms were eligible for study participation (See Supplemental Digital Content 1 for detailed eligibility criteria). This study involves a cross-sectional analysis of the baseline data collected prior to randomization and exposure to treatment.

Measures

Background data. Background information included age, race, sex, and relationship (spouse versus non-spouse) of the dyads as well as caregivers' education level and years in caregiving.

Behavioral symptoms. Behavioral symptoms of interest were derived from the Agitated Behavior in Dementia (ABID) Scale.²⁴

Rejection was assessed by a single item, 'refusing to accept appropriate help'. Four items were identified as reflecting aggressive behaviors ('aggressive to others verbally', 'aggressive to others physically', 'doing things harmful to him/herself', and 'destroying property'). A positive response to any of these items was considered an indication of the presence of one or more aggressive behaviors.

For agitation, we selected 6 items based on Volicer et al.'s⁷ criteria that an agitated-type behavior not involve a caregiving situation or be targeted towards a caregiver ('screaming or crying out inappropriately', 'trying to leave home inappropriately', 'arguing, irritable, or

complaining', 'restless', 'worrying, anxious, or fearful', and 'easily agitated or upset'). For each item, caregivers rated their presence or absence in the past month.

Neurodegeneration associated with dementia. The degree of cognitive impairment in PwD was assessed by Mini-Mental State Examination (MMSE)²⁵ scores (range of 0 to 30) with lower scores indicative of greater cognitive deficits.

Factors associated with PwD. Functional independence was assessed using a 7-item subscale reflecting self-care activities of the psychometrically sound Caregiver Assessment of Function and Upset scale (CAFU),²⁶ For each item (e.g., bathing, dressing, and toileting), caregivers indicated level of assistance required using a 7-point scale (7=*complete independence* to 1=*complete assistance*). A mean score was calculated with higher scores indicating higher independence ($\alpha = 0.92$ for sample).

Pain was measured with 4 items from the Resources for Enhancing Alzheimer's Caregiver Health (REACH) Battery:²⁷ pain over the past few weeks, pain right now, pain at its worst, and pain interfering with the daily activities of PwD. Caregivers were asked to respond to each using a 5-point Likert type scale (1=*not at all* to 5=*extremely*) which was summed for a total pain score ($\alpha=0.88$ for sample).

Factors associated with caregivers. The 12-item Zarit Burden Interview was used to measure caregiver burden on a 5-point scale (0=*never* to 4=*nearly always*).²⁸ Caregivers' responses were summed to represent burden with higher scores indicative of greater burden ($\alpha=0.88$ for sample). For caregiver frustration, a composite score of 8 items (e.g., feeling like screaming/yelling at or hitting/slapping PwD) derived from the REACH II Quality of Care measure was used.²⁷ Caregivers' responses were rated on a 4-point scale from 1 (never) to 4

(always). A mean score was calculated, with high scores indicating greater frustration ($\alpha=0.74$ for sample).

Analysis

Our first aim was to examine the frequency of occurrence of each behavior and their combination. There were 16 missing values in MMSE scores (5.9%). We conducted a chi-square test to examine group differences between missing cases and valid cases for all variables, which indicated that missingness of MMSE scores was not related to outcome variables. Therefore, we decided not to impute missing MMSE values.

A second aim of the study was to examine whether the resulting behavioral cluster subgroups differed by characteristics (PwD age, race, gender, relationship to caregiver; neurodegeneration, pain, functional independence, caregiver burden and frustration) using Kruskal-Wallis (followed by post hoc Mann-Whitney test with Bonferroni correction) and Pearson's χ^2 tests.

A final aim was to investigate the relationship of predictors with each behavioral subgroup using multinomial logistic regression and controlling for the sociodemographic variables described above. In this model, the behavior or subgroup of combined behaviors was the dependent variable, and neurodegeneration, PwD, and caregiver factors were the independent variables. Agitation alone group in which PwDs did not exhibit aggression nor rejection of care was used as a reference group. Results are presented as odds ratios and their 95% confidence intervals (CIs). All analyses were performed with SPSS 22.0 with a two-sided alpha of 0.05.

RESULTS

Of 272, caregivers were primarily female (81%), white (71%), spouses (51%), and well educated (65% > high school). The median age of caregivers was 66.0 years, and provided care

for an average of 3.8 years. PwDs had a median age of 83.0 years, and most were female (54%) and white (71%) with 92% of non-white ($N=73$) being Black/African Americans (Table 1).

Frequency of Behavioral Occurrences

As to behaviors, 247 (91%) reported agitation, 175 (64%) aggression, and 147 (54%) rejection of care. Only 16 (6%) had behavioral symptoms other than these three behaviors. Few PwDs were reported to exhibit only one of the three behaviors: agitation alone ($N=41$, 15%), aggression alone ($N=3$, 1%), and rejection of care alone ($N=5$, 2%).

There was considerable overlap in the occurrences of these three behaviors. Agitation tended to co-occur with other behaviors; 85% ($N=206$) having agitation were also reported to exhibit aggression, rejection of care, or both. Of these, 141 (52%) were reported to exhibit agitation and rejection of care, 171 (63%) were reported to exhibit agitation and aggression, and 106 (39%) all three behaviors.

Given the frequency by which behaviors occurred, we examined four mutually exclusive groups with adequate sample sizes: agitation alone (Agi; $N=41$), agitation and aggression (Agi+Aggr, $N=65$), agitation and rejection of care (Agi+Rej, $N=35$), and all three (All, $N=106$). Thus, in subsequent analyses, we excluded three groups with low sample sizes (rejection of care and aggression ($N=1$), rejection of care alone ($N=5$), and aggression alone ($N=3$)).

Differences between Behavioral Groups

PwD-related Factors: As for sociodemographics, the proportion of female and the median age of PwDs did not differ across the four behavioral groups (Table 3). However, the proportion of white PwDs was significantly lower in those who reportedly exhibited all three behaviors than

those in the other three subgroups (Pearson χ^2 : 11.4, df=3, p=0.01). Fewer white PwDs than nonwhite PwDs were reported to exhibit all three behaviors.

The omnibus test with the four subgroups (Table 3) was significant in relation to level of cognitive impairment of PwD (Kruskal-Wallis test χ^2 : 21.4, df=3, p<0.001). Post-hoc pairwise comparisons showed that MMSE scores were significantly lower in Agi+Rej (MDN=9.0) and All groups (MDN=11.0) compared to Agi (MDN=15.0) or Agi+Aggr (MDN=15.5) .

There was also a significant difference in functional independence of PwD across subgroups (Kruskal-Wallis test χ^2 : 7.85, df=3, p=0.049). A trend was found that functional independence in Agi group (MDN=5.3) was higher than those in Agi+Rej (MDN=4.3) and All (MDN=3.9) groups respectively. The p values for these pairwise associations exceeded 0.05 however. There were no significant differences in PwD pain among behavioral groups.

Caregiver-related Factors: There was a significant difference in caregiver frustration across the four behavioral subgroups (Kruskal-Wallis test χ^2 : 12.76, df=3, p=0.005). Pairwise comparisons revealed a statistically significant difference in frustration level between caregivers in Agi (MDN=1.7) and All (MDN=2.0) group with the latter group reporting greater frustration. There were no significant differences for the proportion of spouse and caregiver burden across different behavioral subgroups.

Predictors of Behavioral Subgroups

PwD-related Factors: Multinomial logistic analyses adjusting for key covariates revealed that higher MMSE scores decreased the odds of belonging to Agi+Rej (OR=0.87, 95% CI=0.84-0.94, Wald χ^2 =11.1, df=1, p=0.001) and All (OR=0.91, 95% CI=0.85-0.97, Wald χ^2 =7.64, df=1,

p=0.006) groups respectively as compared with Agi group (Table 4). Conversely, PwDs with greater cognitive impairment (i.e., lower MMSE scores) were more likely to exhibit rejection of care with or without aggression in addition to agitation behavior.

Caregiver-related Factors: Greater caregiver frustration significantly increased the PwD's odds of belonging to Agi+Aggr (OR=2.96, 95% CI=1.07-8.19, Wald $\chi^2=4.35$, df=1, p=0.037) and All (OR=3.43, 95% CI=1.28-9.20, Wald $\chi^2=6.02$, df=1, p=0.014) groups respectively compared with Agi group. PwD pain, functional independence, and caregiver burden were not significantly associated with behavioral subgroups. No other PwD or caregiver factors were identified as a significant predictor.

DISCUSSION

For this community-based sample, we found that agitation was almost universally reported (91%), followed by aggression (64%) and rejection of care (54%), along with other behavioral symptoms. Examining these three behaviors exclusively however, we identified four distinct groups: caregivers who reported the occurrence of agitation alone (Agi), agitation and aggression (Agi+Aggr), agitation and rejection (Agi+Rej), and all 3 behaviors (All). Of import is that aggression alone, rejection of care alone, and the combination of aggression and rejection of care did not co-occur with much frequency.

For agitation, and consistent with previous studies, we found that 15% of the total sample reported this behavior alone, while aggression and rejection of care rarely occurred independent of other behaviors.^{29,30} PwDs with agitation alone (e.g., no aggression or rejection of care) had the least cognitive impairment (MMSE mean=15.8) and caregiver frustration compared to the other groups, suggesting that PwDs with this behavior alone may be at an early stage of dementia and that caregivers are not initially frustrated.

We found that close to a quarter of this sample (24%) reported a combination of agitation and aggression (Agi+Aggr) suggesting that these two behaviors can occur without rejection for almost a quarter of this sample. As a shortcoming of behavioral symptom measures is an inattention to the context in which a behavior occurs,³¹ it is not possible to determine the way in which this combination of behaviors manifests. Given that rejection of care is not experienced in this group, it may be that it does not occur in the context of providing needed help such as with dressing or bathing.

As to the co-occurrence of agitation and rejection (Agi+Rej), a small percentage (13%) reported this particular combination and no aggression (Agi+Rej). PwDs with this combination had the lowest cognitive status (MMSE mean=9.0) compared to the other three behavioral groups considered, suggesting that agitated behaviors and rejection of needed care may occur as the disease progresses and more hands on care is needed. The positive association between severity of dementia and rejection of care behavior has also been reported previously.³²

We also found that 39% of caregivers reported the co-occurrence of all three behaviors (All), the most frequently occurring combination of behaviors for this sample. The finding that rejection of care and aggression are far more frequently reported together with agitation than independent of each other appears to be consistent with past clinical reports that aggression most often occurs during intimate care in which a PwD may be more likely to manifest this behavior due perhaps to misinterpretation of care attempts or inappropriate care.^{4,7,33,34}

PwDs reported to have all three behaviors were more cognitively and functionally impaired than the other groups except for Agi+Rej in pairwise group comparisons (Table 3), reinforcing that these combinations of behaviors may occur at more advanced disease stage at

least for this sample. Additionally, caregivers reporting managing these three behaviors also reported significantly greater frustration similar to the Agi +Aggression group (Table 3), which aligns with previous studies showing that caregivers reporting many behavioral symptoms are significantly more distressed than those reporting fewer behavioral symptoms.³⁵

The multinomial logistic regression largely confirms these findings. When compared to agitation alone, greater cognitive impairment is a significant predictor of having Agi+Rej and All but not Agi+Aggr (Table 4). This supports the finding that PwDs in Agi+Aggr were significantly less cognitively impaired than those in Agi+Rej and All (Table 3). As PwDs with lower cognitive impairment would not require much assistance if any for instrumental and self-care activities, it would appear that other factors than intimate care precipitate this combination of behaviors.

Another significant predictor of certain combinations of behaviors was greater caregiver frustration which was strongly associated with Agi+Aggr and All but not with Agi+Rej, when compared to Agi. Caregiver frustration in this study captured the extent to which caregivers felt like yelling or screaming or hitting PwD. Since previous research has suggested that a caregiver's negative feelings and attitudes towards a PwD may elicit or exacerbate aggressive behaviors, forming a vicious cycle of abusive communication,^{4,36,37,38} behaviors reported in Agi+Aggr and All may be attributed to caregivers' negative communication style. Conversely, caregivers in Agi+Rej may have used positive communication techniques while interacting with their relatives, thus preventing rejection from escalating into aggression.

Of note is that caregivers reporting the occurrences of all three behaviors differed by race. The proportion of nonwhite PwDs reporting the co-occurrence of all three behaviors was

significantly higher than whites. Although it is unclear why, a prior study similarly showed that the prevalence of dementia-related behaviors was considerably higher in black and Latino PwDs than white/nonhispanic PwDs.³⁹

In sum, the presence of mutually exclusive behavioral subgroups and the different relationships between the subgroups and factors associated with PwDs and caregivers, suggest the need for future research to clearly differentiate among these behaviors and understand the unique precipitating factors of each behavior alone and in combination and their respective impacts on PwD and caregiver wellbeing.

It will be important for future research to further determine the unique combination of predictors for different combinations of behaviors from which to derive targeted interventions that prevent, minimize or manage these behaviors. For example, agitated behaviors that occur outside the context of caregiver interaction may be a response to boredom or loneliness¹⁷ whereas aggression and rejection of care, when they occur during intimate care, may be triggered by ineffective or confrontational communication.^{12,33,38} The former can be managed by social contact and/or structured activity interventions, while the latter can be benefitted from educating caregivers on effective communication techniques.

Our findings suggest that attention should be given to cognitive impairment and caregiver frustration as both were significant predictors of rejection and/or aggression among PwDs who exhibit agitation. Unfortunately, we cannot prevent or reverse cognitive impairment in PwD. However, there are strategies to minimize rejection of care and caregiver frustrations.⁴⁰ In particular, individualized multicomponent interventions involving strategies such as education, skills training, problem solving, stress management, and social support demonstrated

improvements in caregiver stress and emotional well-being as well as behavioral symptoms of PwDs.^{19,27,41,42}

Our results suggest that disease progression may correlate with certain behaviors. While agitation (occurring alone or with aggression) was reported mostly in persons with mild to moderate dementia, rejection of care was reported mainly in persons with moderate to severe dementia (i.e., Agi+Rej and All). It may be that rejection of needed care occurred at the point in which more hands-on care was needed. This finding has implications for caregivers as it suggests that certain behavioral symptoms may occur more frequently at certain disease stages. However, since this is a cross-sectional study and symptoms may be persistent or episodic over time, a longitudinal study is needed to determine the natural course of these behavioral symptoms.

Our findings should be interpreted with caution in light of several limitations. First, data were obtained from caregivers who reported the presence or absence of behaviors versus direct observation. Thus, the reporting of behavioral occurrences may reflect informant bias. However, this limitation is inherent in most studies measuring behaviors in dementia and reflect a challenge clinicians face in a real world practice setting. Second, data were cross-sectional and did not include an understanding of the context in which behaviors occurred. Therefore, a cause-and-effect relationship and careful differentiation of behaviors is not possible. Third, given that caregivers may not apply the same definition to each of the behaviors we considered, there is a possibility that rejection may have been interpreted and reported as agitated or aggressive behavior. Lastly, since this was a descriptive study examining the co-occurrence of behavioral symptoms, groupings of behaviors were not prospectively hypothesized. Therefore, selection of comparison groups was post-hoc and based upon application of definitions of each behavior identified in the literature, versus through factor analysis. Finally, we were unable to include all

theorized potential contributors to behavioral symptoms such as neuropathology, context, premorbid personality, medical conditions, and environmental factors. Future research should investigate the associations of these factors with different behaviors manifested in dementia.

CONCLUSION

Despite these limitations, our study expands prior research by identifying the co-occurrence of three behaviors that have not previously been clearly differentiated and examining factors predicting occurrences. We conclude that agitation, aggression, and rejection are common but distinct behaviors that may overlap or co-occur and in different contexts of care provision. Differentiation of these behaviors and their co-occurrences may require different intervention approaches.

REFERENCES

1. Steinberg M, Shao H, Zandi P, et al. Point and 5-year period prevalence of neuropsychiatric symptoms in dementia: The cache county study. *Int J Geriatr Psychiatry*. 2008;23(2):170-177.
2. Rabins PV, Lyketsos CG, Steele CD. *Practical dementia care*. OUP USA; 2006.
3. Kales HC, Gitlin LN, Lyketsos CG. Assessment and management of behavioral and psychological symptoms of dementia. *BMJ*. 2015;350:h369.
4. Kunik ME, Lynn Snow A, Davila JA, et al. Causes of aggressive behavior in patients with dementia. *J Clin Psychiatry*. 2010;71(9):1145.
5. Cohen-Mansfield J, Billig N. Agitated behaviors in the elderly: I. A conceptual review. *J Am Geriatr Soc*. 1986;34(10):711-721.
6. Patel V, Hope R. Aggressive behaviour in elderly psychiatric inpatients. *Acta Psychiatr Scand*. 1992;85(2):131-135.
7. Volicer L, Bass EA, Luther SL. Agitation and resistiveness to care are two separate behavioral syndromes of dementia. *Journal of the American Medical Directors Association*. 2007;8(8):527-532.
8. Cohen-Mansfield J, Marx MS, Rosenthal AS. A description of agitation in a nursing home. *J Gerontol*. 1989;44(3):M77-84.

9. Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The neuropsychiatric inventory: Comprehensive assessment of psychopathology in dementia. *Neurology*. 1994;44(12):2308-2314.
10. De Medeiros K, Robert P, Gauthier S, et al. The neuropsychiatric inventory-clinician rating scale (NPI-C): Reliability and validity of a revised assessment of neuropsychiatric symptoms in dementia. *International Psychogeriatrics*. 2010;22(06):984-994.
11. Cummings J, Mintzer J, Brodaty H, et al. Agitation in cognitive disorders: International psychogeriatric association provisional consensus clinical and research definition. *International Psychogeriatrics*. 2015;27(01):7-17.
12. Mahoney EK, Hurley AC, Volicer L, et al. Development and testing of the resistiveness to care scale. *Res Nurs Health*. 1999;22(1):27-38.
13. Ishii S, Streim JE, Saliba D. A conceptual framework for rejection of care behaviors: Review of literature and analysis of role of dementia severity. *Journal of the American Medical Directors Association*. 2012;13(1):11-23. e2.
14. Volicer L, Hurley AC. Management of behavioral symptoms in progressive degenerative dementias. *J Gerontol A Biol Sci Med Sci*. 2003;58(9):M837-45.
15. Kong E. Agitation in dementia: Concept clarification. *J Adv Nurs*. 2005;52(5):526-536.
16. Chan D, Kasper JD, Black BS, Rabins PV. Prevalence and correlates of behavioral and psychiatric symptoms in community-dwelling elders with dementia or mild cognitive impairment: The memory and medical care study. *Int J Geriatr Psychiatry*. 2003;18(2):174-182.

17. Cohen-Mansfield J, Werner P, Watson V, Pasis S. Agitation among elderly persons at adult day-care centers: The experiences of relatives and staff members. *International Psychogeriatrics*. 1995;7(03):447-458.
18. Cohen-Mansfield J, Jensen B. Physicians' perceptions of their role in treating dementia-related behavior problems in the nursing home: Actual practice and the ideal. *Journal of the American Medical Directors Association*. 2008;9(8):552-557.
19. Gitlin LN, Winter L, Dennis MP, Hodgson N, Hauck WW. Targeting and managing behavioral symptoms in individuals with dementia: A randomized trial of a nonpharmacological intervention. *J Am Geriatr Soc*. 2010;58(8):1465-1474.
20. Brodaty H, Draper B, Low L. Nursing home staff attitudes towards residents with dementia: Strain and satisfaction with work. *J Adv Nurs*. 2003;44(6):583-590.
21. Cohen-Mansfield J. Nonpharmacologic interventions for inappropriate behaviors in dementia: A review, summary, and critique. *The American Journal of Geriatric Psychiatry*. 2001;9(4):361-381.
22. Volicer L. Behaviors in advanced dementia. *J Am Med Dir Assoc*. 2009;10(2):146; author reply 146-7.
23. Gitlin LN, Winter L, Dennis MP, Hauck WW. A non-pharmacological intervention to manage behavioral and psychological symptoms of dementia and reduce caregiver distress: Design and methods of project ACT3. *Clin Interv Aging*. 2007;2(4):695-703.

24. Logsdon RG, Teri L, Weiner MF, et al. Assessment of agitation in alzheimer's disease: The agitated behavior in dementia scale. *J Am Geriatr Soc*. 1999;47(11):1354-1358.
25. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189-198.
26. Gitlin LN, Roth DL, Burgio LD, et al. Caregiver appraisals of functional dependence in individuals with dementia and associated caregiver upset: Psychometric properties of a new scale and response patterns by caregiver and care recipient characteristics. *J Aging Health*. 2005;17(2):148-171.
27. Belle SH, Burgio L, Burns R, et al. Enhancing the quality of life of dementia caregivers from different ethnic or racial groups: A randomized, controlled trial. *Ann Intern Med*. 2006;145(10):727-738.
28. Bédard M, Molloy DW, Squire L, Dubois S, Lever JA, O'Donnell M. The zarit burden interview a new short version and screening version. *Gerontologist*. 2001;41(5):652-657.
29. Lyketsos CG, Breitner JC, Rabins PV. An evidence-based proposal for the classification of neuropsychiatric disturbance in alzheimer's disease. *Int J Geriatr Psychiatry*. 2001;16(11):1037-1042.
30. Lyketsos CG, Sheppard JE, Steinberg M, et al. Neuropsychiatric disturbance in alzheimer's disease clusters into three groups: The cache county study. *Int J Geriatr Psychiatry*. 2001;16(11):1043-1053.

31. Gitlin LN, Marx KA, Stanley IH, Hansen BR, Van Haitsma KS. Assessing neuropsychiatric symptoms in people with dementia: A systematic review of measures. *International Psychogeriatrics*. 2014;26(11):1805-1848.
32. Volicer L. Toward better terminology of behavioral symptoms of dementia. *Journal of the American Medical Directors Association*. 2012;13(1):3-4.
33. Keene J, Hope T, Fairburn CG, Jacoby R, Gedling K, Ware CJ. Natural history of aggressive behaviour in dementia. *Int J Geriatr Psychiatry*. 1999;14(7):541-548.
34. Ryden MB. Aggressive behavior in persons with dementia who live in the community. *Alzheimer Disease & Associated Disorders*. 1988;2(4):342-355.
35. de Vugt ME, Nicolson NA, Aalten P, Lousberg R, Jolle J, Verhey FR. Behavioral problems in dementia patients and salivary cortisol patterns in caregivers. *J Neuropsychiatry Clin Neurosci*. 2005;17(2):201-207.
36. de Vugt ME, Stevens F, Aalten P, et al. Do caregiver management strategies influence patient behaviour in dementia? *Int J Geriatr Psychiatry*. 2004;19(1):85-92.
37. Ryden MB. Aggressive behavior in persons with dementia who live in the community. *Alzheimer Dis Assoc Disord*. 1988;2(4):342-355.
38. Somboontanont W, Sloane PD, Floyd FJ, Holditch-Davis D, Hogue CC, Mitchell CM. Assaultive behavior in alzheimer's disease: Identifying immediate antecedents during bathing. *J Gerontol Nurs*. 2004;30(9):22-29.

39. Sink KM, Covinsky KE, Newcomer R, Yaffe K. Ethnic differences in the prevalence and pattern of dementia-related behaviors. *J Am Geriatr Soc*. 2004;52(8):1277-1283.
40. Gitlin LN., Piersol, CV. *A caregiver's guide to dementia: Using activities and other strategies to prevent, reduce and manage behavioral symptoms*. 1st ed. Philadelphia, PA: Camino Books, Inc.; 2014.
41. Elliott AF, Burgio LD, Decoster J. Enhancing caregiver health: Findings from the resources for enhancing alzheimer's caregiver health II intervention. *J Am Geriatr Soc*. 2010;58(1):30-37.
42. Gitlin LN, Belle SH, Burgio LD, et al. Effect of multicomponent interventions on caregiver burden and depression: The REACH multisite initiative at 6-month follow-up. *Psychol Aging*. 2003;18(3):361.

SUPPLEMENTAL DIGITAL CONTENT 1. Eligibility criteria. docx

Eligibility criteria for caregivers were 1) living with persons with a physician diagnosis of NINCDS/ADRDA criteria for dementia; 2) being 21 years of age and older; 3) speaking English; 4) planning to live in the area for 6 months; 5) not seeking nursing home placement (within next 6 months); and 7) caregiver report of upset (>5 on a 10-point scale) managing problem behaviors.

Exclusion criteria for PwDs were 1) having a terminal illness with a life expectancy less than 6 months; 2) undergoing active treatments for cancer; 3) having had more than 3 acute hospitalizations in the past year; 4) being involved in another trial regarding problem behaviors; 5) having schizophrenia or bipolar disorder; 6) having dementia related to probable head trauma; and 7) being bed-bound or unresponsive to the environment.

TABLES AND FIGURES

TABLE 1. Demographic Characteristics of 272 Dyads

Characteristics	PwDs (N=272)	Caregivers (N=272)
Age (years), median (IQR)	83.0 (77.0-89.0)	66.0 (57.3-77.0)
Race, N (%)		
White	193 (71)	193 (71)
Non-white	79 (29)	79 (29)
Sex, N (%)		
Female	147 (54)	220 (80.9)
Male	125 (46)	52 (19.1)
Relationship to PwD, N (%)		
Spouse		138 (50.7)
Non-spouse		134 (49.3)
Education, N (%)		
< High school		25 (9.2)
= High school		69 (25.4)
> High school		178 (65.4)
Years caregiving, mean (SD)		3.8 (3.2)

Abbreviation: MMSE = Mini-Mental State Examination; PwD = person with dementia

TABLE 2. Frequency of Number of PwDs Reporting Combinations of Agitation, Aggression, and Rejection of Care

Behavioral Subgroup	N	%
Agitation alone	41	15
Aggression alone	3	1
Rejection of care alone	5	2
Agitation + Aggression	65	24
Aggression + Rejection of care	1	0
Agitation + Rejection of care	35	13
Agitation + Aggression + Rejection of care	106	39
None ^a	16	6
Total	272	100

Notes: PwD = person with dementia

^a PwDs who reportedly exhibited other behaviors than agitation, aggression, or rejection of care (e.g., incontinence, hoarding).

TABLE 3. Characteristics of 272 PwDs and Their Caregivers in Relation to Behavioral Subgroup Categories

Predictors	Range	Overall (N = 247)	Agi† (N = 41)	Agi + Aggr (N = 65)	Agi + Rej (N = 35)	Agi+Aggr+Rej (N = 106)	χ^2 or <i>H</i>	<i>P</i>
Sociodemographics								
PwD age, years, median (IQR)	57 – 101	83 (77-89)	83 (77-90)	82 (74-89)	82 (75-87)	84.5 (80-89)	5.28 ^f	0.153
PwD age, years, mean (SD)	57 – 101	82.4 (8.6)	82.2 (9.5)	80.7 (9.4)	81.1 (9.8)	84.0 (7.2)		
PwD race, white, n (%)		174 (70.4)	32 (78.0)	53 (81.5)	26 (74.3)	63 (59.4)	11.40 ^g	0.010
PwD gender, female, n (%)		136 (55.1)	25 (61.0)	29 (44.6)	21 (60.0)	61 (57.5)	4.06 ^g	0.256
Dyad relationship, spouse, n (%)		119 (48.2)	19 (46.3)	38 (58.5)	19 (54.3)	43 (40.6)	5.79 ^g	0.122
Neurodegeneration factor								
MMSE, median (IQR) ^a	0 - 29	13.0 (6.0-19.0)	15.0 (11.3–21.0)	15.5 (8.8-23.0)	9.0 (0-16.0)	11.0 (5.0-17.0)	21.40 ^f	< .001 ^h
MMSE, mean (SD) ^a	0 - 29	12.8 (8.1) [†]	15.8 (6.6)	15.3 (7.8)	9.0 (8.2)	11.5 (7.9)		
PwD factors								
Pain, median (IQR) ^b	4 - 20	10.0 (7.0-14.0)	11.0 (7.0-14.0)	10.0 (7.0-14.0)	9.0 (6.0-14.0)	10.0 (7.0-14.0)	0.62 ^f	0.893
Pain, mean (SD) ^b	4 - 20	10.5 (4.2)	10.8 (4.2)	10.5 (4.2)	10.1 (4.1)	10.6 (4.2)		
Functional independence, median (IQR) ^c	1 - 7	4.3 (2.9-5.7)	5.3 (3.5-6.0)	4.6 (3.0-6.1)	4.3 (1.9-5.4)	3.9 (2.4-5.3)	7.85 ^f	0.049
Functional independence, mean (SD) ^c	1 - 7	4.1 (1.7)	4.6 (1.8)	4.4 (1.8)	3.8 (1.8)	3.9 (1.6)		
Caregiver factors								
Burden, median (IQR) ^d	1 - 46	21.0 (14.0-29.0)	23.0 (16.3-28.8)	22.0 (13.5-29.0)	22.0 (18.0-26.0)	23.0 (16.8-30.3)	1.16 ^f	0.762
Burden, mean (SD) ^d	1 - 46	22.1 (9.5)	22.7 (8.4)	21.7 (10.0)	21.4 (8.0)	23.0 (9.9)		
Frustration, median (IQR) ^e	1 - 4.5	1.9 (1.6-2.3)	1.7 (1.5-2.1)	2.0 (1.8-2.4)	1.9 (1.6-2.0)	2.0 (1.8-2.4)	12.76 ^f	0.005 ⁱ
Frustration, mean (SD) ^e	1 - 4.5	2.0 (0.5)	1.8 (0.6)	2.0 (0.5)	1.9 (0.4)	2.1 (0.5)		

Notes: Agi = agitation; Aggr = aggression; MMSE = Mini-Mental Status Examination; PwD = person with dementia; Rej = rejection

† N = 232

‡ PwDs who exhibited agitation alone.

^a Lower scores indicate greater cognitive impairment.

^b Higher scores indicate greater pain.

^c Higher scores indicate greater functional independence.

^d Higher scores indicate greater burden.

^e Higher scores indicate greater frustration.

^f Kruskal-Wallis *H*, df = 3 Pearson χ^2 , df = 3

^g Pearson χ^2 , df = 3

^h Significant with Mann-Whitney U post-hoc; contrast 'Agi+Rej'–'Agi+Aggr', 'Agi+Rej'–'Agi', 'All'–'Agi+Aggr', 'All'–'Agi'

ⁱ Significant with Mann-Whitney U post-hoc; contrast 'Agi'–'All'

Table 4. Multinomial Logistic Regression Contrasting the Agitation Alone Group versus the Other Behavioral Groups (N=247)

Predictors	Behavioral Symptoms												
	Agi† (N=41)	Agi + Aggr (N=65)				Agi + Rej (N=35)				Agi + Aggr + Rej (N=106)			
	OR	Wald χ^2 (df)	p	OR	95% CI	Wald χ^2 (df)	p	OR	95% CI	Wald χ^2 (df)	p	OR	95% CI
Neurodegeneration factor													
MMSE	1	0.513 (1)	0.474	0.98	0.91, 1.04	11.092 (1)	0.001	0.87***	0.80, 0.95	7.642 (1)	0.006	0.91**	0.85, 0.97
PwD factors													
Pain	1	0.000 (1)	0.999	1.00	0.90, 1.11	0.009 (1)	0.926	1.01	0.89, 1.13	0.001 (1)	0.977	1.00	0.91, 1.10
Functional independence	1	0.037 (1)	0.848	0.97	0.72, 1.31	0.085 (1)	0.770	1.05	0.75, 1.48	0.052 (1)	0.819	1.03	0.78, 1.37
Caregiver factors													
Burden	1	2.591 (1)	0.107	0.96	0.91, 1.01	0.131 (1)	0.718	0.99	0.93, 1.05	0.576 (1)	0.448	0.98	0.93, 1.03
Frustration	1	4.349 (1)	0.037	2.96*	1.07, 8.19	0.264 (1)	0.607	1.38	0.41, 4.65	6.015 (1)	0.014	3.43*	1.28, 9.20

Notes: These models were adjusted for PwD age, gender, race, and relationship to caregiver.

Agi = agitation; Aggr = aggression; CI = confidence interval; MMSE = Mini-Mental Status Examination; OR = odds ratio; PwD = person with dementia; Rej = rejection of care

χ^2 (27, N = 256) = 56.105, Nagelkerke R^2 = .233, $p < .001$

† Reference group; PwDs who exhibited agitation alone.

* $p < 0.05$; ** $p < 0.01$; *** $p \leq 0.001$

CHAPTER 4: MANUSCRIPT 3

The Impact of Rejection of care, Aggression, and Agitation in Persons with Dementia on Caregiver Depression

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ABSTRACT

Objective: 1) To examine the relationship between three distinct behavioral symptoms (rejection of care, aggression, and agitation) in community-dwelling persons with dementia and caregiver depression and 2) to determine if social support and caregiving mastery each independently moderated this association and for which behavioral symptoms.

Methods: Cross-sectional, secondary analysis using baseline data from two community-based clinical trials. We examined frequency of occurrence of presenting behaviors and their combinations. Multiple logistic regression analyses examined associations between non-overlapping behavioral clusters and caregiver depression. Multiple logistic regression was used to investigate whether social support and

Results: Three symptom clusters (all three behaviors [AOR=2.22, 95% CI=1.02-4.83]), agitation + rejection of care [AOR=2.55, 95% CI=1.06-6.13], agitation + aggression [AOR=2.63, 95% CI=1.17-5.89]) had a positive association with caregiver depression. Agitation alone group did not show any significant association with caregiver depression. Neither social support nor mastery significantly moderated the relationship between behavioral clusters and caregiver depression.

Conclusion: We found that there was a clear difference between agitation alone group and the rest of the behavioral clusters in their associations with caregiver depression. Distinguishing behaviors that are not provoked by caregivers and behaviors that occur when the person with dementia is alone may be important. These results have implications for a potential opportunity to target interventions for caregivers who report unique symptom clusters.

INTRODUCTION

Along with cognitive and functional impairment, behavioral symptoms are increasingly recognized as important aspects of dementia that are of interest to clinicians and researchers. Behavioral symptoms are universal, affecting nearly everyone with dementia at some point in their disease course (Lyketsos et al., 2011). Behavioral symptoms are most problematic for persons with dementia, caregivers, and providers as they are associated with greater caregiver burden (Fischer, Ismail, & Schweizer, 2012), increased risk for nursing home placement (Balesteri, Grossberg, & Grossberg, 2000), prolonged duration of inpatient treatment (Wancata et al., 2003), and decreased quality of life of both persons with dementia and their caregivers (Finkel et al., 1998). Moreover, behavioral symptoms are reported to be more stressful for caregivers than other aspects of the disease such as cognitive and functional declines (Aneshensel et al., 1995; Croog et al., 2006).

Among a variety of behavioral symptoms in dementia, rejection of care, aggression, and agitation are three commonly occurring behaviors that are often grouped together but are not always clearly delineated in the literature (Ishii, Streim, & Saliba, 2012). Authors have argued that it is important to accurately distinguish between these behaviors despite a considerable overlap among them and the lack of consensus definitions (de Medeiros et al., 2010; Ishii et al., 2012; Volicer, Bass, & Luther, 2007). There is also evidence that these three behaviors have a particular pattern in their co-occurrences (e.g., rare independent occurrence of aggression or rejection of care alone without the other behaviors) and that the resulting behavioral clusters (i.e., one or more co-occurring behaviors grouped together) have different relationships with clinical variables (Choi, Budhathoki, & Gitlin, 2017). Despite the evidence for distinction among subsyndromes of these three behaviors, little is known about whether these specifically categorized behavioral clusters differentially impact the caregiver. By taking this approach, which focuses on clearly differentiating these underdefined behaviors, researchers and clinicians could have a potential opportunity to target interventions to better meet the needs of persons with dementia and their caregivers.

Conceptualizing behavioral symptoms through the lens of their impact on caregivers is important in that different types of behaviors (and their co-occurrences) may differentially affect caregivers (Ornstein et al., 2013). For example, caregivers tend to find aggressive behavior (e.g., physical or verbal attacks directed toward caregivers) difficult to deal with, emotionally distressing, and potentially dangerous and as a result they often feel powerless, sad, and ineffective (Hagen, & Sayers, 1995; Zeller et al., 2009). Rejection of care can also distress caregivers in the sense that it interferes with provision of necessary care. Especially spousal caregivers with emotional investment in their relatives may find this behavior more upsetting and disheartening than other behaviors that do not involve caregiving. On the contrary, agitated behaviors that are not directed toward caregivers (e.g., pacing, repetitious mannerisms) may be annoying but not as stressful as aggression or rejection of care to caregivers, resulting in decreased depression. Examining whether specific symptom groups exert differential effects on caregivers can help identify vulnerable caregivers and target treatment strategies.

This study is guided by the stress process model (Aneshensel et al., 1995; Pearlin et al., 1990) which conceptualizes the stress process as having three components. *Stressors* are the challenging conditions experienced by caregivers (e.g., behavioral symptoms in persons with dementia). *Outcomes* refer to the consequences of stressors such as the effects of behavioral symptoms on caregivers' well-being (e.g., depression). *Moderators* are the third component which may serve as buffers of stress. In the literature on stress, social support and mastery (sense of control over one's life circumstances) are generally regarded as protective factors for caregivers' mental health (Haley et al., 1987; Harmell et al., 2011). Stress process model, which focuses on caregiving stress and caregivers' mental health outcomes, specifies these two factors as stress buffers which may attenuate the strength of the relationship between a stressor and an outcome. The framework suggests that the positive relationship between stressors (i.e., behavioral symptoms) and negative consequences (i.e., caregiver depression) can be attenuated by moderating resources (i.e., social support and caregiving mastery) such that the magnitude of the association increases with plentiful socioeconomic resources and decreases with a lack of such resources.

For example, caregivers reporting more social support and/or higher levels of perceived control over the caregiving situation may experience less upset and depression with troublesome behaviors.

The primary aim of this study was to examine the relationship between three distinct behavioral symptoms (rejection of care, aggression, and agitation) in community-dwelling persons with dementia and caregiver depression using baseline data from two clinical trials. The secondary aim was to determine if social support and caregiving mastery each independently moderated this association and for which behavioral symptoms. Earlier stress research indicated that high levels of social support and mastery were related to low levels of caregivers' emotional well-being (Aneshensel et al., 1995; Pearlin et al., 1981; 1990). However, what was measured was the direct buffering effects of these factors. In this study we were interested in examining their conditional effects (i.e., whether certain combinations of behavioral symptoms were especially distressing to caregivers with low levels of resources compared to caregivers with high levels of resources). This study was conceptualized as exploratory and there were no *a priori* hypotheses regarding which behaviors would have more severe effects for caregivers as little is known about individual behavioral symptoms and their impact on caregivers' depressive symptoms. However, we did anticipate that higher social support and feelings of mastery would diminish the impact of behavioral symptom on caregiver depression.

METHODS

Sample

The current study is a secondary analysis of two different community-based datasets that were combined for the purposes of this study: Project ACT (Gitlin et al., 2010a) and COPE (Gitlin et al., 2010b). Project ACT was a randomized controlled trial designed to test the effectiveness of a home-based intervention to minimize targeted behaviors of the persons with dementia. COPE was a 4-month, home-based, nonpharmacological intervention designed to improve functional independence in persons with dementia and caregiver well-being. The present study uses baseline data before randomization and

exposure to the treatment in both trials which included similar measures. The baseline data for a total of 509 dyads (person with dementia-caregivers) were used in analyses.

Participants were recruited in the Philadelphia region between March 2006 and June 2008 (ACT) and between December 2003 and March 2007 (COPE) from media announcements and mailings by social agencies. The inclusion and exclusion criteria of these two trials have been fully described elsewhere (cite). Briefly, caregivers were living with people with a physician diagnosis of NINCDS/ADRDA criteria for dementia or Mini-Mental State Examination (MMSE) (Folstein et al., 1975) score of 23 or less. Caregivers also reported being upset (>5 on a 10-point scale) for managing problem behaviors (ACT) or difficulty managing patient functional decline or behaviors (COPE). Exclusion criteria were terminal illness with a life expectancy less than 9 months, cancer treatments, more than 3 acute hospitalizations in the past year, schizophrenia or bipolar disorder, dementia related to head trauma, and an MMSE score of 0 or being bed-bound.

Measures

Outcome measure. Depressive symptomatology of caregivers was measured using the Center for Epidemiological Studies-Depression Scale (CES-D 10) (Irwin, Artin, & Oxman, 1999). The CES-D 10 is a 10-item measure that asks caregivers about their experience of symptoms related to depression in the past week such as feeling depressed, feeling lonely, and restless sleep. Higher scores on the CES-D 10 indicate greater depressive symptomatology. Caregivers who scored 10 or greater were categorized as being at risk for clinical depression. This scale has been demonstrated to be reliable with good internal consistency (Cronbach's $\alpha = 0.79$) and valid with high construct and concurrent validity ($r = 0.91$).

Behavioral symptoms. Behavioral symptoms were measured by the Agitated Behavior in Dementia Scale (ABID) (Logsdon et al., 1999). ABID is a 16-item caregiver-based rating scale designed to assess commonly observable behaviors in persons with dementia. The measure has excellent internal consistency (0.70), adequate test-retest reliability (ranging from 0.60 to 0.73), and construct validity

confirmed by correlations with other related measures. Each behavior is rated by a caregiver for its presence or absence (yes/no) during the past month. There are no sub-scales or sub-categories for rejection of care, aggression, and agitation provided in the ABID. Therefore dichotomous items were selected and combined to characterize the presence or absence of each behavior. Item selection was mainly based on how the same or similar items are categorized in the Neuropsychiatric Inventory-Clinician (NPI-C) (de Medeiros et al., 2010) rating scale except for rejection of care which is not differentiated from aggression or agitation in NPI-C.

Rejection of care was assessed by a single item, ‘refusing to accept appropriate help.’

Aggression was measured on the basis of four ABID items (‘aggressive to others verbally’, ‘aggressive to others physically’, ‘doing things harmful to him/herself’, and ‘destroying property’). These behaviors have similarly been labeled as aggressive on the NPI-C and other measures. A positive response to any of these items will be considered an indication of the presence of one or more aggressive behaviors.

Agitation was consisted of 6 items (‘screaming or crying out inappropriately’, ‘trying to leave home inappropriately’, ‘arguing, irritable, or complaining’, ‘restless’, ‘worrying, anxious, or fearful’, and ‘easily agitated or upset’). These items have been identified by other measures such as Neuropsychiatric Inventory (NPI) (Cummings et al., 1994) and NPI-C representing this domain of behaviors. In this study we have applied Volicer et al. (2007)’s approach in defining agitation that an agitated-type behavior should not involve a caregiving situation or be targeted towards a caregiver.

Objective stressors. A variety of non-behavior objective stressors were examined. Cognitive status of the person with dementia was assessed using the MMSE and functional status was assessed using the Caregiver Assessment of Function and Upset scale (CAFU) (Gitlin et al., 2005), a 15-item multidimensional measure of functional independence in persons with dementia. Pain of the person with

dementia was assessed using 4 pain-related items of the NIH Resources for Enhancing Alzheimer's Caregiver Health (REACH) (Schulz et al., 2003) battery. Caregivers were asked to rate the pain of the person with dementia: over the past few weeks, right now, pain at its worst, and pain interfering with the daily activities, using a 5-point Likert scale response for each item ranging from "not at all" to "extremely".

Background variables. Person with dementia age, race, gender, and marital status were recorded. Caregiver age, race, gender, marital status, highest level of education, and relationship to the person with dementia were also examined.

Moderator variables. Social support was assessed using a modified version of the Lubben Social Network Scale-Revised (LSNS-R) (Lubben & Gironde, 2004) which is designed to measure perceived social support received by family and friends. This version of scale consists of an equally weighted sum of 13 items used to measure size, closeness, and frequency of contacts of a respondent's social network. A higher score indicates more social support and engagement. The standardized Chronbach coefficient α for the sample was 0.747, indicating acceptable reliability.

Caregiving mastery was assessed by the six-item Caregiving Mastery Index (Lawton et al., 1989) which measures the caregiver's perceived competence in providing care (e.g., "How often do you feel you are able to handle most problems in the care of your care receiver?"). Response options of this 5-point Likert scale range from "never" to "always". Higher scores indicate greater levels of caregiving mastery. Cronbach's α for this scale with our sample was 0.577.

Analysis

We created non-overlapping groups of persons with dementia exhibiting combinations of the three behaviors and examined the association between 4 symptom clusters and caregiver depression using multiple logistic regression analyses. First, the association between each symptom cluster identified by a dummy variable and caregiver depression was examined while controlling for other symptom clusters.

Then the covariates were entered on this model. To determine which variables would be included as covariates, bivariate associations between potential confounders (i.e., background characteristics) and the outcome variable (i.e., caregiver depression) were assessed. Variables which had a significant bivariate relation to the outcome variable at the 0.10 level and were not highly correlated with other variables (correlation > 0.5) were included in the final model. Behavioral clusters that were manifested by less than 2% of the persons with dementia were excluded from the analysis as we judged that to be too small a cluster.

To evaluate moderation effects, we used the approach developed by Baron and Kenny (1986). According to them, the moderator effect can be described as an interaction term between a predictor variable and a moderator variable. A moderator effect is present whenever the interaction is significant. Consistent with the conceptual domain of stress buffering, social support and mastery were considered as moderators that may modify the relationship between stressors (i.e., behavioral symptoms) and caregiver outcome (i.e., depression). The candidate moderator variables (social support and mastery) were dichotomized based on the median of each variable to form “high” and “low” categories (dummy variables) as there were no standard/meaningful cutpoints available. Interaction terms between each behavioral cluster and dummy variable to identify each moderator was created and entered separately as well as simultaneously such that caregiver depression was regressed onto three blocks of variables: behavioral clusters, background characteristics, and a moderator and its interaction term (each of four symptom clusters*dichotomous social support and each of four symptom clusters*dichotomous mastery). All statistical analysis was performed using SPSS ver 24.0 with two-sided alpha of 0.05.

RESULTS

Background Characteristics

Table 1 shows the descriptive and clinical characteristics of the study sample. People with dementia were predominantly women (61.3%), White (71.3%), and, on average, 82.6 years old ($SD = 8.5$). Caregivers were predominantly women (82.9%), White (71.1%), on average, 65.2 years old ($SD = 12.5$), married

(67.2%), and well educated (80.8% > high school). Caregivers were most likely to be husband (33.0%), wife (10.8%), daughter (23.8%), son (2.6%), or other relatives (3.6%).

Behavioral clusters

As summarized in Table 2, behavioral symptoms were reported in the vast majority of persons with dementia (95.1%). Although there was a significant co-occurrence among rejection, aggression, and agitation, we were able to obtain four nonoverlapping symptom clusters based on their co-occurrences. All three behaviors (i.e., rejection of care, aggression, agitation) occurred the most frequently (39.9%) compared to frequency for any one behavior alone or combinations of any two behaviors, followed by agitation + aggression (22.0%), agitation alone (17.9%), and agitation + rejection of care (12.6%). Rejection alone (1.2%), aggression alone (0.8%), and rejection + aggression (0.8%) rarely occurred and were excluded from the final analysis.

Multiple Logistic Regressions Predicting Caregiver Depression

We examined the association of each of the four co-occurring symptom clusters with caregiver depression adjusting for all other symptom clusters, and after simultaneously controlling for covariates (caregiver age, caregiver marital status, and caregiver education) and symptom clusters (Table 3). In both models, each symptom cluster had a positive association with caregiver depression with the exception of agitation alone group, which did not show any significant association with caregiver depression. Among the symptom clusters that had a significant relation with caregiver depression, the magnitude of effects was all in relatively close range (OR between 2.22 and 2.63), with all three (OR = 2.22, $p < 0.05$), agitation + rejection (OR = 2.55, $p < 0.05$), and agitation + aggression (OR = 2.63, $p < 0.05$).

Test of Moderation

No interaction terms were significant at pre-specified $\alpha=0.05$ when they were sequentially entered into the multiple logistic regressions. In the final model, all of the eight interaction terms were added simultaneously (representing combinations of both moderators and behavior clusters), which

showed no significance at alpha of 0.05 either. Therefore, neither social support nor mastery significantly moderated the relationship between behavioral clusters and caregiver depression.

However, social support (OR = 0.43, $p < 0.001$) and mastery (OR = 0.34, $p < 0.001$) each had a negative association with caregiver depression as anticipated, indicating that caregiver social support and mastery may be protective factors for caregiver depression. The correlations between behavioral clusters (except for agitation alone) and caregiver depression remained significant after adjusting for social support or mastery. Yet, in the final model where social support and mastery were simultaneously entered, only agitation + aggression predicted caregiver depression (OR = 2.38, $p < 0.05$) although all three (OR = 2.10, $p = 0.070$) and agitation + rejection (OR = 2.47, $p = 0.052$) both approached the borderline of significance. Also, this final model represents an improvement in Nagelkerke R^2 (0.206) for caregiver depression compared to the first (0.135) and second model (0.162).

DISCUSSION

In this study a variety of clinical variables of dementia including cognitive impairment, functional impairment and pain were examined for their possible relationship with caregiver depression. None of the person with dementia factors were associated with caregiver depression. This finding is consistent with past research which finds that cognitive or functional impairment in the person with dementia was not associated with the caregiver's reported stress (Hooker et al., 2002; Zarit et al., 1980). However, caregiver age, race, and marital status were significant predictors of caregiver depression in this study.

Membership in three behavioral clusters (i.e., all three, agitation + rejection care, agitation + aggression) were associated with greater odds of caregiver depression. Since aggression has been one of the most frequently cited symptoms associated with caregiver depression in the literature (Ornstein & Gaugler, 2012), aggression may have been a driving factor in these associations. Among these three groups agitation + aggression had the strongest effect (OR = 2.63, $p = 0.019$) on caregiver depression when holding all the other predictors constant although the differences in odds ratios were small. This is

the group of caregivers who did not report any rejecting behavior by the person with dementia. The majority of aggressive incidents in persons with dementia occur during personal care provided by caregivers (Keene et al., 1999). Aggression which is not provoked by caregiving activity may be quite stressful for caregivers because caregivers cannot predict such behaviors out of the context. Researchers have suggested that dementia caregivers' increased stress is mainly due to capricious nature of problem behaviors of the person with dementia (Gaugler et al., 2000; McCarty et al., 2000).

It is interesting that agitation + rejection of care group was significantly related to greater likelihood of caregiver depression (OR = 2.55, $p = 0.036$) while agitation only group had no relationship with caregiver depression. The difference between these two groups is just one item asking if the person with dementia refuses care. What makes rejection of care so distressful for caregivers? Research suggests that rejection of care often occurs when the person with dementia does not understand or misunderstands the caregiver's intent to provide care (Volicer et al., 2009). Rejection of care per se may not necessarily disturb the person with dementia unless care is persistently offered or imposed by the caregiver despite the care receiver's rejection. However, it can have tremendous implications for caregivers' mental well-being. Especially for those spousal caregivers who have developed physical and emotional closeness with their counterparts over the lifetime, non-normative behavior such as rejection of care may be a main source of stress as it indicates a major personality change. Moreover, prior research of a population-based sample of older adults caring for a disabled spouse has found that simply being able to give care for a disabled spouse can have beneficial effects on the caregivers. Rejection of care may have deleterious effects on the caregivers' mental health because it takes away the opportunity for them to be supportive of their care receivers.

It should be noted that agitation only group was the only symptom cluster that was not associated with caregiver depression. This may be explained by the 'wear and tear' hypothesis (Townsend et al., 1989) which suggests that caregiver's stress related to management of behavioral symptoms increases over time, resulting in increased risk for depression. Behaviors may have different onsets. Volicer et al.

(2007) reported that agitation was present in a significant number of nursing home residents with borderline intact and mild cognitive impairment while rejection of care was rarely reported in the same sample but its prevalence increased with the increase in severity of cognitive impairment. It is a possibility that those caregivers who reported agitation only may not have cared for their patients long enough to see other challenging behaviors (i.e., rejection of care, aggression). In fact, post-hoc analysis showed that caregivers in the agitation only group had the shortest years of caregiving (3.25 years) of the four behavioral clusters.

It is also possible that agitation may not be as challenging as aggression for caregivers. For example, prior research studies examining predictors of caregiver's negative mental health outcomes has shown that, when aggression and agitation were conceptually separated, aggression was more strongly associated with caregiver depressive symptoms (Danahauer et al., 2004) and caregiver burden (Victoroff et al., 1998) than agitation.

Lastly, the moderation model showed no evidence of a moderating effect of social support and caregiving mastery on the association between behavioral clusters and caregiver depression. This finding is contrary to the assumption of the stress process model. A possible explanation is that the artificial dichotomization that we used to reduce these moderator variables into two categories (i.e., high/low social support or high/low mastery) may have resulted in loss of information (Fitzsimons, 2008). Furthermore, logistic regression may not be an optimal analytical method to test for a moderation effect. There is a possibility that significant moderation effects may test as non-significant interaction coefficients when the dependent variable is subjected to a non-linear transformation (Hess, Hu, & Blair, 2014). Nevertheless, both social support (OR = 0.43, $p < .001$) and caregiving mastery (OR = 0.34, $p < .001$) were found to be significant protective factors for caregiver depression as suggested by the conceptual framework.

The finding that there was a clear difference between agitation only group and the rest of the behavioral clusters in their associations with caregiver depression suggests that distinguishing behaviors

that are not provoked by caregivers and behaviors that occur during caregiver interactions may be very important. To be able to identify caregivers at risk of depression versus those not, researchers should use an assessment tool that conceptualizes behavioral symptoms from the perspective of whether they occur during certain interpersonal interactions.

This finding also implies that caregivers may benefit from trying not to modify care receivers' behaviors if there are no safety concerns. For example, when the person with dementia exhibits pacing behavior, if he or she is in a safe place, a caregiver might just want to let him or her play out the agitation instead of trying to intervene. A caregiver's efforts to manage such behavior, especially when a caregiver tries to forcibly manage them, may result in an argumentative interaction between them, which then might lead to aggressive behavior by the care receiver. However, education on dementia is needed for caregivers to understand that dementia behaviors are a function of the neurodegenerative process and not intended to bother them.

Unlike the progression of cognitive impairment, there are multiple interventions for caregivers to manage behavioral symptoms and increase coping skills. Multicomponent nonpharmacologic treatments including caregiver education and support, training in problem solving, and identifying and addressing underlying causes for specific behaviors have been shown to be effective in managing behavioral symptoms and improving quality of life (Gitlin et al., 2010; Gitlin, Kales, & Lyketsos, 2012). Additionally, a home-based intervention involving care management, referral and linkage, stress reduction techniques, depression education and symptom recognition, and behavioral activation was found to reduce depressive symptoms and enhance quality of life in most older African Americans although these were not dementia caregivers (Gitlin et al., 2013).

Our findings have potential implications for dementia care services and health care professionals. Because symptom clusters have a differential impact on caregiver mental health, those who hope to improve the well-being of dementia caregivers should first distinguish rejection, aggression, and agitation

in persons with dementia, determine the specific combination of behaviors, and then focus intervention efforts on those who are at higher risk for depression (i.e., caregivers who report not only agitated type behaviors but also rejecting and/or aggressive behaviors).

There are several limitations to this study. Because of the cross-sectional design, it is impossible to determine the causal relationships between the behavioral clusters and caregiver depression. There is a possibility that caregiver's depressive state may have increased the potential for behavioral symptoms of the person with dementia. Previous research suggested that caregiver distress and burden may be risk factors of aggressive behaviors of the person with dementia (Kunik et al., 2010). Future studies should include a longitudinal design using repeated measures to understand the intra-individual behavioral changes and to ascertain causal relations behavioral symptoms and the caregiver outcomes. Another limitation of the study is the proxy measure of behavioral symptoms. Our data were based on caregivers' reporting. Besides a potential for recall bias, caregivers' recognition and interpretation of behaviors may have been confounded by their emotional state or cultural beliefs (Stella et al., 2015). Also, there may be other variables that affect the associations. For example, frequency, severity, or appraisal of behavioral symptoms were not examined in this study which may be important predictors of caregivers' depressive symptoms. Lastly, another limitation to note is the brevity and simplicity of rejection of care measure which was measured using a single item. Future work should use a validated and more extensive scale that can clarify distinct components of this behavior.

CONCLUSION

This study suggests that specific symptom clusters of rejection of care, aggression, and agitation may differentially impact caregiver depression. Caregivers who reported the presence of agitated behaviors without the other two behaviors in persons with dementia were not associated with depression while all other behavioral groups were associated with the increased likelihood of caregiver depression. However, it is difficult to determine if some of the behavioral clusters that are associated with caregiver depression exert more impact than others as their associations were similar in magnitude to each other.

These results have implications for a potential opportunity to target interventions for caregivers who report unique symptom clusters. No moderation effects of social support or mastery was found. Our study was exploratory and should be confirmed using validated clinical data with a longitudinal design.

REFERENCES

- Aneshensel, C. S., Pearlin, L. I., Mullan, J. T., Zarit, S. H., & Whitlatch, C. J. (1995). *Profiles in caregiving: The unexpected career*. Academic Press.
- Balestreri, L., Grossberg, A., & Grossberg, G. T. (2000). Behavioral and psychological symptoms of dementia as a risk factor for nursing home placement. *International Psychogeriatrics*, 12(S1), 59-62.
- Baron, R. M., & Kenny, D. A. (1986). The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of personality and social psychology*, 51(6), 1173.
- Choi, S. S. W., Budhathoki, C., & Gitlin, L. N. (2017). Co-occurrence and predictors of three commonly occurring behavioral symptoms in dementia: agitation, aggression, and rejection of care. *The American Journal of Geriatric Psychiatry*, 25(5), 459-468.
- Croog, S. H., Burleson, J. A., Sudilovsky, A., & Baume, R. M. (2006). Spouse caregivers of Alzheimer patients: problem responses to caregiver burden. *Aging and Mental Health*, 10(2), 87-100.
- Cummings, J. L., Mega, M., Gray, K., Rosenberg-Thompson, S., Carusi, D. A., & Gornbein, J. (1994). The Neuropsychiatric Inventory comprehensive assessment of psychopathology in dementia. *Neurology*, 44(12), 2308-2308.
- Danhauer, S. C., McCann, J. J., Gilley, D. W., Beckett, L. A., Bienias, J. L., & Evans, D. A. (2004). Do behavioral disturbances in persons with Alzheimer's disease predict caregiver depression over time?. *Psychology and Aging*, 19(1), 198.
- De Medeiros, K., Robert, P., Gauthier, S., Stella, F., Politis, A., Leoutsakos, J., ... & Geda, Y. E. (2010). The Neuropsychiatric Inventory-Clinician rating scale (NPI-C): reliability and validity of a

- revised assessment of neuropsychiatric symptoms in dementia. *International Psychogeriatrics*, 22(6), 984-994.
- Finkel, S. I., e Silva, J. C., Cohen, G. D., Miller, S., & Sartorius, N. (1998). Behavioral and psychological symptoms of dementia: A consensus statement on current knowledge and implications for research and treatment. *The American Journal of Geriatric Psychiatry*, 6(2), 97-100.
- Fischer, C. E., Ismail, Z., & Schweizer, T. A. (2012). Delusions increase functional impairment in Alzheimer's disease. *Dementia and geriatric cognitive disorders*, 33(6), 393-399.
- Fitzsimons, Gavan J. (2008), "[Death to Dichotomizing](#)," *Journal of Consumer Research*, 35(1), 5-8.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *Journal of psychiatric research*, 12(3), 189-198.
- Gaugler, J. E., Edwards, A. B., Femia, E. E., Zarit, S. H., Stephens, M. A. P., Townsend, A., & Greene, R. (2000). Predictors of institutionalization of cognitively impaired elders: Family help and the timing of placement. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, 55(4), P247-P255.
- Gitlin, L. N., Roth, D. L., Burgio, L. D., Loewenstein, D. A., Winter, L., Nichols, L., ... & Martindale, J. (2005). Caregiver appraisals of functional dependence in individuals with dementia and associated caregiver upset: psychometric properties of a new scale and response patterns by caregiver and care recipient characteristics. *Journal of aging and health*, 17(2), 148-171.
- Gitlin, L. N., Winter, L., Dennis, M. P., Hodgson, N., & Hauck, W. W. (2010a). Targeting and managing behavioral symptoms in individuals with dementia: a randomized trial of a nonpharmacological intervention. *Journal of the American Geriatrics Society*, 58(8), 1465-1474.

- Gitlin, L. N., Winter, L., Dennis, M. P., Hodgson, N., & Hauck, W. W. (2010b). A biobehavioral home-based intervention and the well-being of patients with dementia and their caregivers: the COPE randomized trial. *Jama*, 304(9), 983-991.
- Gitlin, L. N., Kales, H. C., & Lyketsos, C. G. (2012). Nonpharmacologic management of behavioral symptoms in dementia. *Jama*, 308(19), 2020-2029.
- Gitlin, L. N., Harris, L. F., McCoy, M. C., Chernett, N. L., Pizzi, L. T., Jutkowitz, E., ... & Hauck, W. W. (2013). A Home-Based Intervention to Reduce Depressive Symptoms and Improve Quality of Life in Older African Americans A Randomized Trial. *Annals of internal medicine*, 159(4), 243-252.
- Hagen, B. F., & Sayers, D. (1995). When caring leaves bruises: The effects of staff education on resident aggression. *Journal of gerontological nursing*, 21(11), 7-9.
- Haley, W. E., Levine, E. G., Brown, S. L., & Bartolucci, A. A. (1987). Stress, appraisal, coping, and social support as predictors of adaptational outcome among dementia caregivers. *Psychology and aging*, 2(4), 323.
- Harmell, A. L., Chattillion, E. A., Roepke, S. K., & Mausbach, B. T. (2011). A review of the psychobiology of dementia caregiving: A focus on resilience factors. *Current psychiatry reports*, 13(3), 219-224.
- Hess, J. D., Hu, Y., & Blair, E. (2014). On testing moderation effects in experiments using logistic regression. Unpublished paper. Available at SSRN: <https://ssrn.com/abstract=2393725> or <http://dx.doi.org/10.2139/ssrn.2393725>
- Hooker, K., Bowman, S. R., Coehlo, D. P., Lim, S. R., Kaye, J., Guariglia, R., & Li, F. (2002). Behavioral change in persons with dementia: Relationships with mental and physical health of

- caregivers. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, 57(5), P453-P460.
- Irwin, M., Artin, K. H., & Oxman, M. N. (1999). Screening for depression in the older adult: criterion validity of the 10-item Center for Epidemiological Studies Depression Scale (CES-D). *Archives of internal medicine*, 159(15), 1701-1704.
- Ishii, S., Streim, J. E., & Saliba, D. (2012). A conceptual framework for rejection of care behaviors: review of literature and analysis of role of dementia severity. *Journal of the American Medical Directors Association*, 13(1), 11-23.
- Keene, J., Hope, T., Fairburn, C. G., Jacoby, R., Gedling, K., & Ware, C. J. (1999). Natural history of aggressive behaviour in dementia. *International journal of geriatric psychiatry*, 14(7), 541-548.
- Kunik, M. E., Snow, A. L., Davila, J. A., Steele, A. B., Balasubramanyam, V., Doody, R. S., ... & Morgan, R. O. (2010). Causes of aggressive behavior in patients with dementia. *The Journal of clinical psychiatry*, 71(9), 1145-1152.
- Lawton, M. P., Kleban, M. H., Moss, M., Rovine, M., & Glicksman, A. (1989). Measuring caregiving appraisal. *Journal of Gerontology*, 44(3), P61-P71.
- Logsdon, R. G., Teri, L., Weiner, M. F., Gibbons, L. E., Raskind, M., Peskind, E., ... & Thai, L. J. (1999). Assessment of agitation in Alzheimer's disease: the agitated behavior in dementia scale. *Journal of the American Geriatrics Society*, 47(11), 1354-1358.
- Lubben, J., & Gironde, M. (2004). Measuring social networks and assessing their benefits. *Social networks and social exclusion: Sociological and policy perspectives*, 20-34.
- Lyketsos, C. G., Carrillo, M. C., Ryan, J. M., Khachaturian, A. S., Trzepacz, P., Amatnick, J., ... & Miller, D. S. (2011). Neuropsychiatric symptoms in Alzheimer's disease.

- McCarty, H. J., Roth, D. L., Goode, K. T., Owen, J. E., Harrell, L., Donovan, K., & Haley, W. E. (2000). Longitudinal course of behavioral problems during Alzheimer's disease: Linear versus curvilinear patterns of decline. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 55(4), M200-M206.
- Ornstein, K., & Gaugler, J. E. (2012). The problem with “problem behaviors”: a systematic review of the association between individual patient behavioral and psychological symptoms and caregiver depression and burden within the dementia patient–caregiver dyad. *International Psychogeriatrics*, 24(10), 1536-1552.
- Ornstein, K., Gaugler, J. E., Devanand, D. P., Scarmeas, N., Zhu, C., & Stern, Y. (2013). The differential impact of unique behavioral and psychological symptoms for the dementia caregiver: how and why do patients' individual symptom clusters impact caregiver depressive symptoms?. *The American Journal of Geriatric Psychiatry*, 21(12), 1277-1286.
- Pearlin, L. I., Menaghan, E. G., Lieberman, M. A., & Mullan, J. T. (1981). The stress process. *Journal of Health and Social behavior*, 337-356.
- Pearlin, L. I., Mullan, J. T., Semple, S. J., & Skaff, M. M. (1990). Caregiving and the stress process: An overview of concepts and their measures. *The gerontologist*, 30(5), 583-594.
- Schulz, R., Burgio, L., Burns, R., Eisdorfer, C., Gallagher-Thompson, D., Gitlin, L. N., & Mahoney, D. F. (2003). Resources for Enhancing Alzheimer's Caregiver Health (REACH): overview, site-specific outcomes, and future directions. *The Gerontologist*, 43(4), 514-520.
- Stella, F., Forlenza, O. V., Laks, J., Andrade, L. P., Castilho Cação, J., Govone, J. S., ... & Lyketsos, C. G. (2015). Caregiver report versus clinician impression: disagreements in rating neuropsychiatric symptoms in Alzheimer's disease patients. *International journal of geriatric psychiatry*, 30(12), 1230-1237.

- Townsend, A., Noelker, L., Deimling, G., & Bass, D. (1989). Longitudinal impact of interhousehold caregiving on adult children's mental health. *Psychology and aging*, 4(4), 393.
- Victoroff, J., Mack, W. J., & Nielson, K. A. (1998). Psychiatric complications of dementia: impact on caregivers. *Dementia and Geriatric Cognitive Disorders*, 9(1), 50-55.
- Volicer, L., Bass, E. A., & Luther, S. L. (2007). Agitation and resistiveness to care are two separate behavioral syndromes of dementia. *Journal of the American Medical Directors Association*, 8(8), 527-532.
- Volicer, L., Van der Steen, J. T., & Frijters, D. H. (2009). Modifiable factors related to abusive behaviors in nursing home residents with dementia. *Journal of the American Medical Directors Association*, 10(9), 617-622.
- Wancata, J., Windhaber, J., Krautgartner, M., & Alexandrowicz, R. (2003). The consequences of non-cognitive symptoms of dementia in medical hospital departments. *The International Journal of Psychiatry in Medicine*, 33(3), 257-271.
- Zarit, S. H., Reever, K. E., & Bach-Peterson, J. (1980). Relatives of the impaired elderly: correlates of feelings of burden. *The gerontologist*, 20(6), 649-655.
- Zeller, A., Hahn, S., Needham, I., Kok, G., Dassen, T., & Halfens, R. J. (2009). Aggressive behavior of nursing home residents toward caregivers: a systematic literature review. *Geriatric Nursing*, 30(3), 174-187.

TABLES AND FIGURES

TABLE 1. Characteristics of the Sample (N=509)

Characteristic	Person with dementia (PwD)	Caregiver (CG)
Age, mean \pm SD, years	82.6 \pm 8.5	65.2 \pm 12.5
Gender (female), %	61.3	82.9
Race, %		
White	71.3	71.1
African-American	26.5	26.5
Other	2.2	2.4
Education (years)		
High school or less		19.3
Some college		28.1
College or more		52.7
Marital status (married), %	47.9	67.2
Kin relationship of CG to PwD, %		
Husband		33.0
Wife		10.8
Son		2.6
Daughter		23.8
Other		3.6
Unknown		26.3

TABLE 2. Proportion of Persons with Dementia Experiencing Combinations of Behavioral Symptoms

Behavior Cluster	Frequency	Percentage
All three	203	39.9
Agitation + Rejection	64	12.6
Agitation + Aggression	112	22.0
Rejection + Aggression	4	0.8
Rejection only	6	1.2
Aggression only	4	0.8
Agitation only	91	17.9
None	25	4.9

Notes: Percentages are based on the total sample (N=509).

TABLE 3. Summary of Multiple Logistic Regression Analyses Predicting Caregiver Depression (N=509)

	Model 1 ^a			Model 2 ^b		
	AOR	<i>p</i>	95% CI	AOR	<i>p</i>	95% CI
All three	2.47	0.018	1.17-5.23	2.22	0.043	1.02-4.83
Agitation + Rejection	2.71	0.022	1.16-6.36	2.55	0.036	1.06-6.13
Agitation + Aggression	2.73	0.013	1.24-6.02	2.63	0.019	1.17-5.89
Agitation only	1.38	0.441	0.61-3.13	1.24	0.613	0.54-2.89
Caregiver age				1.01	0.134	1.00-1.03
Caregiver marital status				0.68	0.068	0.45-1.03
Caregiver education						
High school or less				-	0.002	-
Some college				0.48	0.003	0.30-0.79
College or more				0.55	0.006	0.36-0.84
Nagelkerke R Square		0.033			0.086	

Notes:

^a Adjusted for other behavior symptom clusters without covariates

^b Adjusted for other behavior symptom clusters and covariates (CG age, CG marital status, and CG education)

AOR = adjusted odds ratio; CI = confidence interval

TABLE 4. The Moderating Effect of Social Support and Mastery on the Association Between Behavioral Clusters and Caregiver Depression (N=509)

	Model 1 ^a			Model 2 ^b			Model 3 ^c		
	AOR	<i>p</i>	95% CI	AOR	<i>p</i>	95% CI	AOR	<i>P</i>	95% CI
All three	2.29	0.039	1.04-5.00	2.05	0.078	0.92-4.56	2.10	0.07	0.94-4.70
Agitation + Rejection	2.76	0.025	1.13-6.71	2.29	0.072	0.93-5.65	2.47	0.052	0.99-6.15
Agitation + Aggression	2.56	0.024	1.13-5.79	2.42	0.037	1.05-5.56	2.38	0.043	1.03-5.50
Agitation only	1.21	0.660	0.52-2.83	1.09	0.841	0.46-2.61	1.07	0.881	0.45-2.57
Caregiver age	1.01	0.148	1.00-1.03	1.01	0.133	1.00-1.03	1.01	0.157	1.00-1.03
Caregiver marital status	0.71	0.116	0.47-1.09	0.63	0.032	0.41-0.96	0.65	0.056	0.42-1.01
Caregiver education									
High school or less	-	0.002	-	-	0.025	-	-	0.030	-
Some college	0.49	0.004	0.30-0.80	0.54	0.017	0.33-0.90	0.55	0.022	0.33-0.92
College or more	0.54	0.006	0.35-0.84	0.64	0.045	0.41-0.99	0.63	0.046	0.40-0.99
Moderator 1: Social support	0.43	0.000	0.30-0.62		NA		0.43	0.000	0.29-0.63
Moderator 2: Mastery		NA		0.34	0.000	0.24-0.50	0.34	0.000	0.23-0.50
Nagelkerke R Square		0.135			0.162			0.206	

Notes:

All models were adjusted for other behavioral symptom clusters and covariates (CG age, CG marital status, and CG education) simultaneously. None of the interaction terms (i.e., each of the 4 behavioral clusters*social support, each of the 4 behavioral clusters*mastery) was significant and therefore interaction terms were dropped from the models.

^a Adjusted for social support

^b Adjusted for mastery

^c Adjusted for both social support and mastery simultaneously

AOR = adjusted odds ratio; CI = confidence interval

CHAPTER 5: DISCUSSION

The purpose of this dissertation was fourfold: 1) to investigate the extent to which behaviors co-occur in one study and whether the combination and frequency by which they co-occur can be replicated in another caregiver sample; 2) to examine the predictors of individual behavioral symptoms and their combinations (e.g., agitation alone; agitation plus aggression; agitation plus rejection of care; all three behaviors); 3) to investigate whether individual behavioral symptoms and/or their combinations have a differential impact on caregiver depressive symptomatology; and 4) to examine whether social support and caregiving mastery moderate the impact of behavioral symptoms on caregiver depression within each behavioral cluster. The main findings are summarized here by the following specific aims:

Aim 1 - Determine whether rejection of care, aggression and agitation occur independently of the other and also the extent to which they co-occur in persons with dementia living in the community (ACT trial data).

Of 272, 247 (91%) reported agitation, 175 (64%) aggression, and 147 (54%) rejection of care. Only 16 (6%) had behavioral symptoms other than these three behaviors. Few PwDs were reported to exhibit only one of the three behaviors: agitation alone (N=41, 15%), aggression alone (N=3, 1%), and rejection of care alone (N=5, 2%).

There was considerable overlap in the occurrences of these three behaviors. Agitation tended to co-occur with other behaviors; 85% (N=206) having agitation were also reported to exhibit aggression, rejection of care, or both. Of these, 141 (52%) were reported to exhibit agitation and rejection of care, 171 (63%) were reported to exhibit agitation and aggression, and 106 (39%) all three behaviors.

Given the frequency by which behaviors occurred, we examined four mutually exclusive groups with adequate sample sizes: agitation alone (Agi; N=41), agitation and aggression (Agi+Aggr, N=65), agitation and rejection of care (Agi+Rej, N=35), and all three (All, N=106). Thus, in subsequent analyses,

we excluded three groups with low sample sizes (rejection of care and aggression (N=1), rejection of care alone (N=5), and aggression alone (N=3) (Table 1).

TABLE 1. Frequency of Number of PwDs Reporting Combinations of Agitation, Aggression, and Rejection of Care

Behavioral Subgroup	N	%
Agitation alone	41	15
Aggression alone	3	1
Rejection of care alone	5	2
Agitation + Aggression	65	24
Aggression + Rejection of care	1	0
Agitation + Rejection of care	35	13
Agitation + Aggression + Rejection of care	106	39
None ^a	16	6
Total	272	100

Notes: PwD = person with dementia

^a PwDs who reportedly exhibited other behaviors than agitation, aggression, or rejection of care (e.g., incontinence, hoarding).

Aim 2 - Evaluate whether the behavioral clusters differ with regard to factors associated with persons with dementia (cognitive impairment, ADL function, pain) and their caregivers (frustration and burden) (ACT trial data).

PwD-related Factors: Multinomial logistic analyses adjusting for key covariates revealed that higher MMSE scores decreased the odds of belonging to Agi+Rej (OR=0.87, 95% CI=0.84-0.94, Wald $\chi^2=11.1$, df=1, p=0.001) and All (OR=0.91, 95% CI=0.85-0.97, Wald $\chi^2=7.64$, df=1, p=0.006) groups respectively as compared with Agi group (Table 4). Conversely, PwDs with greater cognitive impairment (i.e., lower MMSE scores) were more likely to exhibit rejection of care with or without aggression in addition to agitation behavior (Table 2).

Caregiver-related Factors: Greater caregiver frustration significantly increased the PwD's odds of belonging to Agi+Aggr (OR=2.96, 95% CI=1.07-8.19, Wald $\chi^2=4.35$, df=1, p=0.037) and All (OR=3.43, 95% CI=1.28-9.20, Wald $\chi^2=6.02$, df=1, p=0.014) groups respectively compared with Agi group. PwD

pain, functional independence, and caregiver burden were not significantly associated with behavioral subgroups. No other PwD or caregiver factors were identified as a significant predictor (Table 2).

TABLE 2. Multinomial Logistic Regression Contrasting the Agitation Alone Group versus the Other Behavioral Groups (N=247)

Predictors	Behavioral Symptoms												
	Agi† (N=41)		Agi + Aggr (N=65)			Agi + Rej (N=35)			Agi + Aggr + Rej (N=106)				
	OR	Wald χ^2 (df)	p	OR	95% CI	Wald χ^2 (df)	p	OR	95% CI	Wald χ^2 (df)	p	OR	95% CI
Neurodegeneration factor													
MMSE	1	0.513 (1)	0.474	0.98	0.91, 1.04	11.092 (1)	0.001	0.87***	0.80, 0.95	7.642 (1)	0.006	0.91**	0.85, 0.97
PwD factors													
Pain	1	0.000 (1)	0.999	1.00	0.90, 1.11	0.009 (1)	0.926	1.01	0.89, 1.13	0.001 (1)	0.977	1.00	0.91, 1.10
Functional independence	1	0.037 (1)	0.848	0.97	0.72, 1.31	0.085 (1)	0.770	1.05	0.75, 1.48	0.052 (1)	0.819	1.03	0.78, 1.37
Caregiver factors													
Burden	1	2.591 (1)	0.107	0.96	0.91, 1.01	0.131 (1)	0.718	0.99	0.93, 1.05	0.576 (1)	0.448	0.98	0.93, 1.03
Frustration	1	4.349 (1)	0.037	2.96*	1.07, 8.19	0.264 (1)	0.607	1.38	0.41, 4.65	6.015 (1)	0.014	3.43*	1.28, 9.20

Notes: These models were adjusted for PwD age, gender, race, and relationship to caregiver.

Agi = agitation; Aggr = aggression; CI = confidence interval; MMSE = Mini-Mental Status Examination; OR = odds ratio; PwD = person with dementia; Rej = rejection of care

χ^2 (27, N = 256) = 56.105, Nagelkerke R^2 = .233, $p < .001$

† Reference group; PwDs who exhibited agitation alone.

* $p < 0.05$; ** $p < 0.01$; *** $p \leq 0.001$

Aim 3 - Determine if the prevalence of behavioral clusters identified in a sample from one trial (ACT) can be replicated in another sample of community-dwelling persons with dementia (COPE).

As can be seen in Table 3, the proportions of cluster occurrences between ACT and COPE were quite comparable with rare occurrences of three behavioral clusters (rejection + aggression, rejection only, and aggression only; all ≤ 5 in frequency counts) observed in both data sets.

TABLE 3. Comparison of Proportions of Persons with Dementia Experiencing Combinations of Behavioral Symptoms between ACT and COPE

Behavior Cluster	Project ACT		Project COPE	
	Frequency	Percentage	Frequency	Percentage
All three	106	39.0	97	40.9
Agitation + Rejection	35	12.9	29	12.2
Agitation + Aggression	65	23.9	47	19.8
Rejection + Aggression	1	0.4	3	1.3
Rejection only	5	2.0	1	0.4
Aggression only	3	1.8	1	0.4
Agitation only	41	15.1	50	21.1
None	16	5.9	9	3.8
Total	272	100.0	237	100.0

Aim 4 – Assess whether behavioral clusters have a differential impact on caregiver depression after controlling for potential confounders (e.g., background characteristics of dyads, cognitive status, functional status, etc.). Upon positive finding of Aim 3, ACT and COPE data sets will be combined for this analysis.

Based on the positive finding of Aim 3, ACT and COPE data sets were combined for the analysis of Aims 4 and 5. The baseline data for a total of 509 dyads (person with dementia-caregivers) were used in analyses. We examined the association of each of the four co-occurring symptom clusters with caregiver depression adjusting for all other symptom clusters, and after simultaneously controlling for covariates (caregiver age, caregiver marital status, and caregiver education) and symptom clusters (Table 4). In both models, each symptom cluster had a positive association with caregiver depression with the exception of agitation alone group, which did not show any significant association with caregiver depression. Among the symptom clusters that had a significant relation with caregiver depression, the

magnitude of effects was all in relatively close range (OR between 2.22 and 2.63), with all three (OR = 2.22, $p < 0.05$), agitation + rejection (OR = 2.55, $p < 0.05$), and agitation + aggression (OR = 2.63, $p < 0.05$).

TABLE 4. Summary of Multiple Logistic Regression Analyses Predicting Caregiver Depression (N=509)

	Model 1 ^a			Model 2 ^b		
	AOR	<i>p</i>	95% CI	AOR	<i>p</i>	95% CI
All three	2.47	0.018	1.17-5.23	2.22	0.043	1.02-4.83
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Some college				0.48	0.003	0.30-0.79
College or more				0.55	0.006	0.36-0.84
Nagelkerke R Square		0.033			0.086	

Notes:

^a Adjusted for other behavior symptom clusters without covariates

^b Adjusted for other behavior symptom clusters and covariates (CG age, CG marital status, and CG education)

AOR = adjusted odds ratio; CI = confidence interval

Aim 5 – Investigate whether the association between behavioral clusters and caregiver depression is moderated by psychosocial resources (social support and caregiving mastery).

Interaction between each behavioral cluster and social support and mastery respectively as predictors of caregiver depression was assessed. No interaction terms were significant at pre-specified $\alpha=0.05$ when they were sequentially entered into the multiple logistic regressions (data not shown). In the final model, all of the eight interaction terms were added simultaneously (representing combinations of both moderators and behavior clusters), which showed no significance at α of 0.05 either. Therefore, neither social support nor mastery significantly moderated the relationship between behavioral clusters and caregiver depression.

LIMITATIONS AND STRENGTHS

This dissertation has several limitations. First, direct measurement of behavioral symptoms cannot be ascertained. Behavioral data in this study are based on caregiver's report versus direct observation. This informant-based measurement of behaviors may be influenced by a number of factors such as inaccurate recall of behavioral episodes, caregiver's mental state (e.g., frustration, burden), caregiver's prior relationship with person with dementia, and environmental variables. However, since direct observation of behavioral episodes would be very difficult, this should be considered as an inherent drawback of most dementia caregiver and behavior studies.

Second, it is unclear how caregivers define and/or perceive each behavior or distinguish between behavioral symptoms. Rejection of care may be perceived by some caregivers as an agitated or aggressive behavior. Behaviors such as screaming, pushing, or hitting which can occur during intimate ADL care (i.e., rejection of care) may also be perceived and reported as verbal agitation and/or physical aggression depending on the caregiver/staff and the context in which behaviors are triggered. Thus, there is a possibility that definitions of behavioral symptoms were not consistently applied within and/or between caregivers/staff.

Third, there are unmeasured potential contributors of behavioral symptoms. Neurobiological basis of behavioral symptoms has been investigated as a possible contributor by neuroscientists using neuroimaging technology (Banno et al., 2014; Kales et al., 2015). It is theorized that behavioral symptoms could result from the disconnection or disruption to the network between various brain regions responsible for behaviors and emotions (Kales et al., 2015). The current study did not examine these factors. Also excluded from the study were environmental factors such as level of stimulation or level of activity. They were not originally measured in the data set, and this is an inherent limitation related to a secondary data analysis.

Lastly, generalizability may be a problem. The study population of ACT and COPE is a non-probability convenience sample of participants from the metropolitan area who contacted the research

team in response to media announcements and mailings by social agencies. A preliminary analysis of the baseline data revealed that persons with dementia of the combined data set of ACT and COPE are predominantly female (59%), white (70%), and with average mental state scores indicating moderate to severe dementia (MMSE mean=13, SD=8). Therefore, it is possible that the participants in ACT and COPE may not represent all persons with dementia and their caregivers living in the community in the U.S.

Despite these limitations, there are a few notable strengths. First, this is the first study of which we are aware that systematically and rigorously examines the co-occurrences, predictors, and differential impact on caregiver depression of rejection of care, aggression, and agitation in persons with dementia in the community. Thus, the finding that clusters of co-occurring behaviors of rejection of care, aggression, and agitation have different relationships with various clinical variables is a major contribution to the literature.

Another strength of this dissertation study is that this study used two different samples to examine the same phenomena. The fact that the frequency of behavioral clusters identified in one sample was replicated in another sample of community-dwelling persons with dementia increases the validity of the findings as to the co-occurrences of rejection of care, aggression, and agitation in this population. Consequently, the two data sets were combined to provide a sufficiently large sample for examining the aims 4 and 5 of this dissertation.

Overall, this dissertation study expanded prior research by highlighting a differentiation among rejection, aggression, and agitation and the influence of one behavioral cluster relative to others on important clinical variables.

IMPLICATIONS

This research has several important implications. Under our second aim, we found that a modifiable factor (i.e., caregiver frustration) was associated with the occurrence of certain combinations of rejection, aggression, and agitation. Thus, interventions that can help the caregiver to cope with his or

her frustration (e.g., problem solving skills, communications strategies) are needed to prevent or manage these behavioral symptoms (Gitlin et al., 2012). Further, it will be important for future research to further determine the unique combination of predictors for different combinations of behaviors from which to derive targeted interventions that prevent, minimize, or manage these behaviors.

The finding under the fourth aim that there was a clear distinction between agitation only group and the rest of the behavioral clusters in their associations with caregiver depression suggests that differentiating behaviors that are not provoked by caregivers and behaviors that occur during caregiver interactions may be very important. To be able to identify caregivers at risk of depression versus those not, researchers should use an assessment tool that conceptualizes behavioral symptoms from the perspective of whether they occur during an interpersonal interaction or when the person with dementia is alone.

This finding also implies that caregivers may benefit from trying not to modify care receivers' behaviors if there are no safety concerns. For example, when the person with dementia exhibits pacing behavior, if he or she is in a safe place, a caregiver might just want to let him or her play out the agitation instead of trying to intervene. A caregiver's efforts to manage such behavior, especially when a caregiver tries to forcibly manage them, may result in an argumentative interaction between them, which then might lead to aggressive behavior by the care receiver.

Although the moderation model under our fifth aim showed no evidence of a moderating effect of social support and caregiving mastery on the association between behavioral clusters and caregiver depression, it should be noted that there are inherent limitations related to the use of logistic regression and artificial dichotomization for testing of a moderation effect (Fitzsimons, 2008). Thus, future research should continue to explore the relationship among these factors using a method that properly reflects moderation effects, that is, a procedure that does not subject the dependent variable to a non-linear transformation (Hess et al., 2014).

Lastly, this study showed that subgroups of persons with dementia exhibiting different combinations of co-occurring behaviors (i.e., behavioral clusters of rejection, aggression, and agitation) have different relationships with the contributory factors and caregiver outcome. This finding is particularly important for clinical trials testing effectiveness of a pharmacological and/or nonpharmacological interventions since the intervention may be effective against one behavioral cluster but not the other. The first step to developing successful targeted interventions should be to accurately measure these behaviors, which suggests the need for future research to recognize rejection of care, aggression, and agitation as separate clinical constructs and clearly differentiate these behaviors in clinical measurements.

CONCLUSION

The current study provides convincing evidence that community-dwelling persons with dementia exhibiting rejection of care, aggression, and agitation can be grouped into distinct combinations of these behaviors. Although these are overlapping behaviors, their combinations appear to have different relationships with various factors related to the person with dementia and the caregiver, and differential impact on caregiver outcome. Greater cognitive impairment was associated with ‘agitation + rejection of care’ and ‘all three behaviors’ clusters while greater caregiver frustration was associated with ‘agitation + aggression’ and ‘all three behaviors’ clusters. In addition, ‘all three behaviors’, ‘agitation + rejection’, and ‘agitation + aggression’ each had a positive association with caregiver depression whereas ‘agitation alone’ had no such association. The findings in this study support clear distinction among rejection of care, aggression, and agitation.

REFERENCES for Chapter 5

- Banno, K., Nakaaki, S., Sato, J., Torii, K., Narumoto, J., Miyata, J., ... Akechi, T. (2014). Neural basis of three dimensions of agitated behaviors in patients with Alzheimer disease. *Neuropsychiatric Disease and Treatment*, 10, 339–348. <https://doi.org/10.2147/NDT.S57522>
- Fitzsimons, Gavan J. (2008), “Death to Dichotomizing,” *Journal of Consumer Research*, 35(1), 5-8.
- Gitlin, L. N., Kales, H. C., & Lyketsos, C. G. (2012). Nonpharmacologic management of behavioral symptoms in dementia. *Jama*, 308(19), 2020-2029.
- Hess, J. D., Hu, Y., & Blair, E. (2014). On testing moderation effects in experiments using logistic regression. Unpublished paper. Available at
SSRN: <https://ssrn.com/abstract=2393725> or <http://dx.doi.org/10.2139/ssrn.2393725>
- Kales, H. C., Gitlin, L. N., & Lyketsos, C. G. (2015). Assessment and management of behavioral and psychological symptoms of dementia. *BMJ (Clinical Research Ed.)*, 350, h369. <https://doi.org/10.1136/bmj.h369>

APPENDICES

Appendix 1- Agitated Behavior in Dementia Scale (ABID)

CR Behavioral Occurrence and Caregiver Upset

Now I will ask some questions about your (CR's) behavior. These are similar to the questions we asked on the phone. For each I will ask if the behavior occurs, and how many times it occurred within the past month. Also, if it did occur, I'll ask how much it bothered or upset you. (If yes, show card #13 for b.)

(Reference: 2x/day=60 times; daily=30 times; 1x/week=4 times; 2x/week=8 times; 3x/week=12 times; 4x/week=16 times; 5x/week=20 times; 6x/week=24 times)

If CG cannot give a number after probing, write "constant".

1. Within the past month, has your (CR) been aggressive to others verbally? aggv

No 0 ()

Yes 1a.() How many times has this occurred (in the past month)? __aggvx__

1b.How bothered or upset were you by this? aggvb

Not at

Moderately

Extremely

2. Within the past month, has (CR) been aggressive to others physically? aggp

No 0 ()

Yes 2a.() How many times has this occurred (in the past month)? __aggpx__

2b.How bothered or upset were you by this? aggpb

Not at

Moderately

Extremely

*IF CG REPORTS AGGRESSIVE BEHAVIOR OCCURRED AND SCORES 3+ ON UPSET, ASK:
Would you like some help with this right away?*

No 0 ()

Yes 1 () fasthlp

*IF YES, REFER CG TO HIS/HER OWN PHYSICIAN AND INSTRUCT HIM/HER TO
CONTACT PHYSICIAN RIGHT AWAY.*

*INDICATE THAT PROJECT DIRECTOR OR DESIGNATE WILL BE CONTACTING HIM/HER
TO FOLLOW-UP. COMPLETE ALERT DOCUMENTATION AND GIVE TO APPROPRIATE
SITE PERSONNEL.*

3. Within the past month, has your (CR) been doing things harmful to him/herself?

No 0 ()

Yes 3a.() How many times has this occurred (in the past month)? __hrtsx__

3b.How bothered or upset were you by this? hrtsb

Not at

Moderately

Extremely

4. Within the past month, has your (CR) been screaming or crying out inappropriately?

No 0 ()

Yes 4a.() How many times has this occurred (in the past month)? __cryx__

4b.How bothered or upset were you by this? cryb

Not at

Moderately

Extremely

5. Within the past month, has your (CR) been destroying property?

No 0 ()

Yes 5a.() How many times has this occurred (in the past month)? __despx__

5b.How bothered or upset were you by this? despb

Not at

Moderately

Extremely

6. Within the past month, has your (CR) been refusing to accept appropriate help or resisting care with daily activities such as dressing, bathing, or eating?

No 0 ()

Yes 6a.() How many times has this occurred (in the past month)? __refusx__

6b.How bothered or upset were you by this? refusb

Not at

Moderately

Extremely

7. Within the past month, has your (CR) been trying to leave home inappropriately (i.e., wandering)? wander

No 0 ()

Yes 7a.() How many times has this occurred (in the past month)? _wanderx

7b.How bothered or upset were you by this? wanderb

Not at

Moderately

Extremely

8. Within the past month, has your (CR) been arguing, irritable, or complaining?

No 0 ()

argu

Yes 8a.() How many times has this occurred (in the past month)? _argux__

8b.How bothered or upset were you by this? argub

Not at

Moderately

Extremely

9. Within the past month, has your (CR) engaged in inappropriate sexual behavior?

No 0 ()

insex

Yes 9a.() How many times has this occurred (in the past month)? __insexx_

9b.How bothered or upset were you by this? insexb

Not at

Moderately

Extremely

10. Within the past month, has your (CR) been engaging in socially inappropriate behavior?

No 0 ()

insoc

Yes 10a.() How many times has this occurred (in the past month)? _insocx_

10b.How bothered or upset were you by this? insocb

Not at

Moderately

Extremely

11. Within the past month, has your (CR) been restless? rest

No 0 ()

Yes 11a.() How many times has this occurred (in the past month)? _restx__

11b.How bothered or upset were you by this? restb

Not at

Moderately

Extremely

12. Within the past month, has your (CR) been worrying, anxious or fearful? anx

No 0 ()

Yes 12a.() How many times has this occurred (in the past month)? __anxx__

12b.How bothered or upset were you by this? anxb

Not at

Moderately

Extremely

13. Within the past month, has your (CR) been easily agitated or upset? agit

No 0 ()

Yes 13a.() How many times has this occurred (in the past month)? _agitx__

13b.How bothered or upset were you by this? agitb

Not at

Moderately

Extremely

14. Within the past month, has your (CR) been waking and getting up at night? wak

No 0 ()

Yes 14a.() How many times has this occurred (in the past month)? _wakx__

14b.How bothered or upset were you by this? wakb

Not at

Moderately

Extremely

15. Within the past month, has your (CR) had distressing beliefs not founded in reality (i.e., delusions)? delus

No 0 ()

Yes 15a.() How many times has this occurred (in the past month)? _delusx_

15b.How bothered or upset were you by this? delusb

Not at

Moderately

Extremely

16. Within the past month, has your (CR) been seeing, hearing, or sensing distressing things or people that were not real (i.e., hallucinations) ? halluc

No 0 ()

Yes 16a.() How many times has this occurred (in the past month)? _hallucx_

16b.How bothered or upset were you by this? hallucb

Not at

Moderately

Extremely

Appendix 2 - Center for Epidemiologic Studies Depression Scale (CES-D)

This section deals with statements people might make about how they feel. For each of the statements, please indicate how often you felt that way during the past week. (Show card #15)

	Rarely or none of the time	Some or a little of the time	Occasionally or a moderate amount of time	Most or almost all of the time	Unknown	<i>Refused</i>
	(<1 day)	(1-2 days)	(3-4 days)	(5-7 days)		
1. I felt that everything that I did was an effort effort	0 ()	1 ()	2 ()	3 ()	-3 ()	-4 ()
2. My sleep was restless. sleep	0 ()	1 ()	2 ()	3 ()	-3 ()	-4 ()
3. I felt depressed. depres	0 ()	1 ()	2 ()	3 ()	-3 ()	-4 ()
4. I was happy. happy	0 ()	1 ()	2 ()	3 ()	-3 ()	-4 ()
5. I felt lonely. flone	0 ()	1 ()	2 ()	3 ()	-3 ()	-4 ()
6. People were unfriendly. unfri	0 ()	1 ()	2 ()	3 ()	-3 ()	-4 ()
7. I enjoyed life. enjoy	0 ()	1 ()	2 ()	3 ()	-3 ()	-4 ()
8. I felt sad. fsad	0 ()	1 ()	2 ()	3 ()	-3 ()	-4 ()
9. I felt that people disliked me. dislk	0 ()	1 ()	2 ()	3 ()	-3 ()	-4 ()
10. I could not get going. going	0 ()	1 ()	2 ()	3 ()	-3 ()	-4 ()

Curriculum Vitae

Part I

PERSONAL DATA

Scott Seung W. Choi, RN

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Email: schoi51@jhu.edu

EDUCATION

2013-present PhD program, Johns Hopkins University School of Nursing, Baltimore, MD

2012 BSN, University of North Carolina at Chapel Hill School of Nursing,
Chapel Hill, NC

2008 MA in Advertising, Michigan State University, East Lansing, MI

CURRENT LICENSE AND CERTIFICATION

2013-present RN, State of Maryland Board of Nursing #R210442

PROFESSIONAL EXPERIENCE

2016-present	Research Coordinator	Dept. of Community Public Health, Johns Hopkins University School of Nursing
2015-present	Staff RN, Psychiatry	Meyer 3, Johns Hopkins Hospital, Baltimore, MD
2012-2013	Staff RN, Med/Surg	6 Neurosciences, UNC Hospitals, Chapel Hill, NC

2003-2006	Assistant Manager	Marketing, Harley-Davidson Motor Company, Seoul, Korea
1997-2000	Sr. KATUSA Sergeant	52 nd Medical Battalion, U.S. Army, Seoul, Korea

HONORS AND AWARDS

2016	Dean's Travel and Conference Fund, \$500
2016	GAPNAF 2016 Research Project Grant, \$2,000
2016	STTI Nu Beta Chapter 2016 Nursing Research Award, \$1,500
2014-2016	JHUSON Graduate Research Assistantship
2013-2014	Johns Hopkins University School of Nursing Scholarship
2009	Top 3 Paper Award, ICA Organizational Communication Division
2008-2009	Rutgers University Graduate Teaching Assistantship
2000	U.S. Army Commendation Medal

RESEARCH

2016-present	Research Coordinator, PI: Hae-Ra Han
2014-2016	Research Assistant, PI: Laura N. Gitlin
2013-2014	Research Residency, PI: Laura N. Gitlin

Curriculum Vitae

Part II

SCHOLARSHIP

Gitlin, L. N., Hodgson, N. A., **Choi, S.** & Marx, K. (in press). Interventions to Address Functional Decline in Persons with Dementia: Closing the Gap Between What a Person “Does Do” and What They “Can Do” Chapter in Randolph W. Parks, Ronald F. Zec, Ph.D., Mark W. Bondi, Ph.D. and Angela L. Jefferson, Ph.D. (eds) in *Neuropsychology of Alzheimer’s Disease and Other Dementias*, 2nd Edition, Oxford University Press.

Choi, S. S. W., Budhathoki, C., & Gitlin, L. N. (2016). Co-occurrence and predictors of three commonly occurring behavioral symptoms in dementia: agitation, aggression, and rejection of care. *The American Journal of Geriatric Psychiatry*. doi: 10.1016/j.jagp.2016.10.013. [Epub ahead of print]

Gitlin, L. N., Hodgson, N. A., & **Choi, S. S. W.** (2016). Home-Based Interventions Targeting Persons with Dementia: What Is the Evidence and Where Do We Go from Here?. In *Dementia Care* (pp. 167-188). Springer International Publishing.

Walther, J.B., Carr, C., **Choi, S.**, DeAndrea, D., Kim, J., Tong, S.T., & Van Der Heide, B. (2010). Interaction of interpersonal, peer, and media influence sources online: A research agenda for technology convergence. In Z. Papacharissi (Ed.), *A networked self: Identity, community and culture on social network sites* (pp. 17-38). New York: Routledge.

Podium Presentations

Choi, S.W., Budhathoki, C., Volicer, L., & Gitlin, L.N. *The differential impact of rejection of care, aggression, and agitation on dementia caregivers’ depressive symptoms*. Paper presented at the 36th Annual Gerontological Advanced Practice Nurses Association Conference, Nashville, TN.

Choi, S.W., Budhathoki, C., Volicer, L., & Gitlin, L.N. *Co-occurrence and predictors of agitation, aggression, and rejection of care in dementia*. Paper presented at the 21st IAGG World Congress of Gerontology and Geriatrics, San Francisco, CA.

Choi, S.W., Budhathoki, C., & Gitlin, L.N., (2015). *Correlates of rejection of care, agitation, and aggression in community dwelling older adults with dementia*. Gerontological Society of America, 68th Annual Scientific Meeting, Orlando, FL.

Choi, S.W., Kim, K.H., & Gitlin, L.N., (2014). Rejection of care, agitation, aggression – Distinct but overlapping behaviors. In B.R. Hansen (Chair), *Understanding Behavioral Symptoms in Persons with Dementia: Characteristics, Associations, and Measurement*. Symposium conducted at the Gerontological Society of America, 67th Annual Scientific Meeting, Washington, D.C.

Kim, Y. H., & Choi, S. (2010, June). *The effect of discursive anonymity on language use in computer-mediated communication*. Paper presented at the annual convention of the International Communication Association, Singapore.

Scott, C. R., & **Choi, S.** (2009, May). *Communication policies in the workplace: Tensions surrounding identifiability and anonymity of technology users*. Paper presented at the annual convention of the International Communication Association, Chicago, IL. [Top Paper Panel in Organizational Communication]

In Preparation

Choi, S.W., Budhathoki, C., & Gitlin, L.N. (dissertation manuscript, in preparation). The differential impact of rejection of care, aggression, and agitation on dementia caregivers' depressive symptoms.

Choi, S.W., Budhathoki, C., Volicer, L., & Gitlin, L.N. (in preparation). Co-occurrence and Predictors of Agitation, Aggression, and Rejection of Care in Dementia.

Choi, S.W., Cajita, M., & Gitlin, L.N. (in preparation). Measurement of rejection of care, aggression, and agitation in persons with dementia: A systematic review of measures.

EDUCATIONAL ACTIVITIES

Fall 2017	Clinical Instructor, Public Health Nursing, 112 hours of Clinical Practicum, Master's level, 7 students, The Johns Hopkins University School of Nursing, Baltimore, MD
Spring 2016	Guest Lecturer, Topic: Dementia, Promoting Health in Older Adults, Master's level, 110 students, The Johns Hopkins University School of Nursing, Baltimore, MD
Spring 2016	Teaching Assistant, JHUSON, master's level course, 55 students
Fall 2014	Graduate Biostatistics Tutor, JHUSON, 10 PhD students

PROFESSIONAL ACTIVITIES

- 2016–present Gerontological Advanced Practice Nurses Association, member
- 2015–present Sigma Theta Tau International (STTI), member
- 2014–present Gerontological Society of America, member, abstract reviewer
- 2016–present *International Association of Gerontology and Geriatrics (IAGG)*, member

OTHER ACTIVITIES

Invited Participant, United States Young Leaders Discussion Series for Innovative Ideas to Address Dementia, United Kingdom Science and Innovation Network, American Association for the Advancement of Science, Washington, DC, February 9, 2015

Student Ambassador, Summer Research Institute, Center for Innovative Care in Aging, The Johns Hopkins University School of Nursing, Baltimore, MD, June 2014, June 2015, & June 2016

Volunteer RN, The Luke Charity Clinic, Raleigh, NC, Jun 2012 – Jun 2013

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Born February 9, 1977
Seoul, South Korea